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     (FILE 'HOME' ENTERED AT 15:22:31 ON 02 FEB 2004)
               SET COST OFF

     FILE 'HCAPLUS' ENTERED AT 15:22:50 ON 02 FEB 2004
                E ALBUMIN/CT
L1           753 S E3
L2           132 S E11
                E E47+ALL
L3         80101 S E2+NT
                E E33+ALL
L4           566 S E3,E2
L5         25218 S E2+NT
L6        157881 S ?ALBUMIN?
L7        181833 S L1-L6
L8          2969 S BDNF OR BD NF
L9          2881 S BRAIN DERIVED NEUROTROPHIC FACTOR
L10         2883 S (BD OR BRAIN DERIVED)()(NF OR NEUROTROPHIC FACTOR)
                E NEUROTROPHIC FACTOR/CT
L11          141 S E10
L12         2554 S E26
                E E25+ALL
L13          789 S E3-E5 AND BRAIN DERIVED
L14          679 S E12,E13
L15         3242 S E2+NT (L) BRAIN DERIVED
L16           64 S L7 AND L8-L15
L17        19234 S INTERFERONALPHA OR ALPHAINTERFERON OR INTERFERONBETA OR BETAI
                E INTERFERON/CT
L18          302 S E3-E19
L19        18390 S E85-E101
                E INTERFERONS/CT
                E E3+ALL
L20        18391 S E7,E6 (L) (ALPHA OR BETA)
L21          546 S L7 AND L17-L20
L22         2340 S TIMP()(I OR 1)

     FILE 'REGISTRY' ENTERED AT 15:29:36 ON 02 FEB 2004
L23            1 S 140208-24-8

     FILE 'HCAPLUS' ENTERED AT 15:30:37 ON 02 FEB 2004
L24         2026 S L23
L25          859 S TISSUE INHIBITOR(1W)METALLOPROTEINASE 1
L26           27 S METALLOPROTEINASE INHIBITOR 1
L27          651 S TIMP1
L28           12 S FIBROBLAST COLLAGENASE INHIBITOR
L29           91 S L7 AND L22,L24-L28
L30          678 S L16,L21,L29
L31         9815 S IFNALPHA OR IFNBETA OR ALPHAIFN OR BETAIFN OR IFN(A)(ALPHA OR
L32          119 S L7 AND L31
L33          700 S L30,L32
L34           62 S L33 AND (FUSION OR FUSE OR FUSED OR FUSES OR FUSING)
L35          167 S L33 AND RECOMBIN?
L36           44 S L33 AND CHIMER?
L37          202 S L34-L36
                E ROSEN C/AU
L38           27 S E3,E4
                E ROSEN CRAIG/AU
L39          625 S E3-E5
                E HASELTINE W/AU
L40          302 S E3,E4,E7-E10
L41           10 S L33 AND L38-L40
                E HUMAN GENOME SCI/PA,CS
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L42          975 S E5-E37
L43           13 S L33 AND L42
L44           13 S L41,L43
L45           13 S L44 AND L37
L46            9 S L45 AND (SHELFLIFE OR SHELF LIFE)
L47            4 S L45 NOT L46
                 SEL DN AN 1 4
L48            2 S L47 NOT E1-E6
L49           11 S L46,L48
                 SEL RN
                 DEL SEL
                 E FUSION PROTEIN/CT
L50        11933 S E9
                 E E9+ALL
L51         3795 S E3,E4
L52            5 S L51 AND L33
L53           29 S L50 AND L33
L54           34 S L49,L52,L53
L55           27 S L54 AND ALBUMIN
L56            7 S L54 NOT L55
L57          159 S L37 AND ALBUMIN
L58          132 S L57 NOT L43-L49,L52-L56
L59            6 S L58 AND L16
L60            7 S L58 AND L29
L61          121 S L58 NOT L59,L60
L62           96 S L61 AND (PD<=20000412 OR PRD<=20000412 OR AD<=20000412)
                 SEL DN AN 9 12 13 24 29 31 35 39 44 47 55 58 72 74 83 85 92 93
L63           18 S L62 AND E1-E54
L64           29 S L49,L63 AND L1-L22,L24-L63
L65           29 S L64 AND ?ALBUMIN?
L66           29 S L64 AND (INF? OR INTERFERON OR TIMP? OR NEUROTROPHIC?)

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 16:00:16 ON 02 FEB 2004
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FILE COVERS 1907 - 2 Feb 2004  VOL 140 ISS 6
FILE LAST UPDATED: 1 Feb 2004  (20040201/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


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L66  ANSWER 1 OF 29  HCAPLUS  COPYRIGHT 2004 ACS on STN
AN   2003:571103  HCAPLUS
DN   139:122690
ED   Entered STN:  25 Jul 2003
TI   Albumin fusion proteins for prolonged shelf-life of therapeutic proteins
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IN Ballance, David James; Turner, Andrew John; Rosen, Craig A.; Haseltine, William A.
PA Human Genome Sciences, Inc., USA; Delta Biotechnology Limited; Principia Pharmaceutical Corporation
SO PCT Int. Appl., 598 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N
CC 63-3 (Pharmaceuticals)
Section cross-reference(s): 3
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003060071	A2	20030724	WO 2002-US40891	20021223

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI	US 2001-341811P	P	20011221
	US 2002-350358P	P	20020124
	US 2002-351360P	P	20020128
	US 2002-359370P	P	20020226
	US 2002-360000P	P	20020228
	US 2002-367500P	P	20020327
	US 2002-370227P	P	20020408
	US 2002-378950P	P	20020510
	US 2002-382617P	P	20020524
	US 2002-383123P	P	20020528
	US 2002-385708P	P	20020605
	US 2002-394625P	P	20020710
	US 2002-398008P	P	20020724
	US 2002-402131P	P	20020809
	US 2002-402708P	P	20020813
	US 2002-411355P	P	20020918
	US 2002-411426P	P	20020918
	US 2002-414984P	P	20021002
	US 2002-417611P	P	20021011
	US 2002-420246P	P	20021023
	US 2002-423623P	P	20021105

AB The present invention encompasses albumin fusion proteins. Many therapeutic proteins in their native state or when recombinantly produced are typically labile mols. exhibiting short shelf-lives, particularly when formulated in aqueous solns.; fusions of the therapeutic protein with human serum albumin have a longer serum half-life and/or stabilized activity in solution (or in a pharmaceutical composition) in vitro and/or in vivo than the corresponding unfused therapeutic mols. Thus, albumin fusion proteins are provided comprising granulocyte colony-stimulating factor, interleukin 2, parathormone, erythropoietin, interferon β, interferon α2, interferon A/D hybrid, a single-chain insulin analog, growth hormone, and (7-36)GLP-1. Nucleic acid mols. encoding the albumin fusion proteins of the invention are also encompassed by the invention, as are vectors containing these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the albumin fusion proteins of the invention and using these nucleic acids, vectors, and/or host cells. Addnl. the present invention encompasses pharmaceutical compns. comprising albumin fusion proteins and methods of treating or preventing diseases,

disorders or conditions related to diabetes mellitus using albumin fusion proteins of the invention.

ST albumin fusion therapeutic protein shelflife

IT Animal cell line
(293, recombinant expression host; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Animal cell line
(CHO, recombinant expression host; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Animal cell line
(NSO, recombinant expression host; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiviral, T1249 peptide inhibitor derived from HIV-1; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Antidiabetic agents
Human
Linking agents
Molecular cloning
(human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Fusion proteins (chimeric proteins)
Interleukin 2
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Signal peptides
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Animal cell
(mammalian, recombinant expression host; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Diabetes mellitus
(non-insulin-dependent, treatment of; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Protein sequences
(of human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Plasmid vectors
(pC4; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Plasmid vectors
(pEE12.1; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Plasmid vectors
(pSAC35; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Saccharomyces cerevisiae
Yeast
(recombinant expression host that is glycosylation and protease-deficient; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Albumins, biological studies
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(serum; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Interferons
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(α2; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Interferons
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(α; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Interferons
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(αAD; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT Interferons
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(β; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT 562119-52-2P 562119-53-3P 562119-54-4P 562119-55-5P 562119-56-6P
562119-57-7P 562119-58-8P 562119-59-9P 562119-60-2P 562119-61-3P
562119-62-4P 562119-63-5P 562119-64-6P 562119-65-7P 562119-66-8P
562119-67-9P 562119-68-0P 562119-69-1P 562119-70-4P 562119-71-5P
562119-72-6P 562119-73-7P 562119-74-8P 562119-75-9P 562119-76-0P
562119-77-1P 562119-78-2P 562119-79-3P 562119-80-6P 562119-81-7P
562119-82-8P 562119-83-9P 562119-85-1DP, Albumin (human), subfragments, fusion products
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT 9002-64-6P, Parathormone 9004-10-8P, Insulin, biological studies
11096-26-7P, Erythropoietin 89750-14-1P, Glucagon-like peptide I
143011-72-7P, Granulocyte colony-stimulating factor
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT 562119-84-0
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(nucleotide sequence; human serum albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

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RL: PRP (Properties)
(unclaimed nucleotide sequence; albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

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RL: PRP (Properties)
(unclaimed nucleotide sequence; albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

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RL: PRP (Properties)
(unclaimed nucleotide sequence; albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT 562137-51-3 562137-52-4 562137-53-5 562137-54-6 562137-55-7
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RL: PRP (Properties)
(unclaimed nucleotide sequence; albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT 562126-87-8 562126-88-9 562126-89-0 562126-90-3 562126-91-4
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RL: PRP (Properties)
(unclaimed protein sequence; albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

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RL: PRP (Properties)
(unclaimed protein sequence; albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

IT 2543-43-3 16941-32-5, Glucagon (swine) 16960-16-0, α1-24-Corticotropin 33017-11-7, Proinsulin C-peptide (human) 40958-31-4, Somatostatin (sheep reduced) 62087-72-3 65505-61-5 75306-06-8, Somatostatin-28 (sheep reduced) 82177-09-1 85482-68-4 85734-71-0 91917-63-4, Atrial natriuretic peptide-28 (human reduced) 110543-54-9 118934-21-7 119777-39-8 122024-47-9 125677-89-6 130912-02-6 131748-18-0 131748-19-1 134374-28-0 147613-04-5 155709-76-5 166980-40-1 170098-75-6 177339-71-8 192503-43-8 197520-45-9 247166-37-6 263906-58-7 283148-45-8 313951-59-6 367273-46-9 367273-47-0 367273-48-1 404935-01-9 477953-25-6 477953-26-7 477953-27-8 477953-28-9 477953-29-0 477953-30-3 477953-31-4 477953-32-5 477953-33-6 477953-34-7 477953-35-8 478188-11-3 478188-13-5 561304-79-8 561304-80-1 561304-81-2 561304-86-7 561304-88-9 561304-92-5 562077-29-6 562077-30-9 562077-31-0 562077-32-1 562077-33-2 562077-34-3 562077-35-4 562077-36-5 562077-37-6 562077-38-7 562077-39-8 562077-40-1 562077-41-2
RL: PRP (Properties)
(unclaimed sequence; albumin fusion proteins for prolonged shelf-life of therapeutic proteins)

L66 ANSWER 2 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:571004 HCAPLUS
DN 139:122689
ED Entered STN: 25 Jul 2003
TI **Albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins
IN **Rosen, Craig A.; Haseltine, William A.**
PA **Human Genome Sciences, Inc., USA**
SO PCT Int. Appl., 1086 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K
CC 63-3 (Pharmaceuticals)
Section cross-reference(s): 3
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003059934	A2	20030724	WO 2002-US40892	20021223

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI	US 2001-341811P	P	20011221
	US 2002-350358P	P	20020124
	US 2002-359370P	P	20020226
	US 2002-360000P	P	20020228
	US 2002-367500P	P	20020327
	US 2002-370227P	P	20020408
	US 2002-378950P	P	20020510
	US 2002-398008P	P	20020724
	US 2002-402131P	P	20020809
	US 2002-402708P	P	20020813
	US 2002-411355P	P	20020918
	US 2002-414984P	P	20021002
	US 2002-417611P	P	20021011

US 2002-420246P P 20021023
US 2002-423623P P 20021105

AB The present invention encompasses **albumin fusion** proteins. Many therapeutic proteins in their native state or when **recombinantly** produced are typically labile mols. exhibiting short **shelf-lives**, particularly when formulated in aqueous solns.; **fusions** of the therapeutic protein with human serum **albumin** have a longer serum half-life and/or stabilized activity in solution (or in a pharmaceutical composition) in vitro and/or in vivo than the corresponding unfused therapeutic mols. Thus, **albumin fusion** proteins are provided comprising **interferon** . **beta.**, **interferon** α 2, insulin, bone morphogenetic protein 9, glucagon-like peptide-I(7-36), a hybrid **interferon** A/D, and extendin 4. Nucleic acid mols. encoding the **albumin fusion** proteins of the invention are also encompassed by the invention, as are vectors containing these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the **albumin fusion** proteins of the invention and using these nucleic acids, vectors, and/or host cells. Addnl. the present invention encompasses pharmaceutical compns. comprising **albumin fusion** proteins and methods of treating or preventing diseases, disorders or conditions related to diabetes mellitus using **albumin fusion** proteins of the invention.

ST **albumin fusion** therapeutic protein **shelflife**

IT Animal cell line
(293, **recombinant** expression host; human serum **albumin fusion** proteins for prolonged **shelf -life** of therapeutic proteins)

IT Animal cell line
(CHO, **recombinant** expression host; human serum **albumin fusion** proteins for prolonged **shelf -life** of therapeutic proteins)

IT Animal cell line
(NSO, **recombinant** expression host; human serum **albumin fusion** proteins for prolonged **shelf -life** of therapeutic proteins)

IT Metabolism, animal
(disorder, treatment of; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)

IT Antidiabetic agents
Antiobesity agents
Cardiovascular agents
Human
Linking agents
Molecular cloning
(human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)

IT **Fusion proteins (chimeric proteins)**
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)

IT Signal peptides
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)

IT Diabetes mellitus
(insulin-dependent, treatment of; human serum **albumin fusion** proteins for prolonged **shelf-life** of

therapeutic proteins)

IT Animal cell
(mammalian, **recombinant** expression host; human serum **albumin fusion** proteins for prolonged **shelf -life** of therapeutic proteins)

IT Nerve, disease
(neuropathy, treatment of; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)

IT Diabetes mellitus
(non-insulin-dependent, treatment of; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)

IT Protein sequences
(of human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)

IT Plasmid vectors
(pC4; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)

IT Plasmid vectors
(pEE12.1; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)

IT Plasmid vectors
(pSAC35; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)

IT Saccharomyces cerevisiae
Yeast
(**recombinant** expression host that is glycosylation and protease-deficient; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)

IT Eye, disease
(retinopathy, treatment of; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)

IT **Albumins, biological studies**
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(serum; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)

IT Cardiovascular system, disease
Endocrine system, disease
Heart, disease
Hyperglycemia
Kidney, disease
Nervous system, disease
Obesity
(treatment of; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)

IT **Interferons**
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(α **2**; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)

IT **Interferons**
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(α ; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic

proteins)

IT **Interferons**
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(α **AD**; human serum **albumin** **fusion** proteins for prolonged **shelf-life** of therapeutic proteins)

IT **Interferons**
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(β ; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)

IT 75306-06-8, Somatostatin-28 (sheep reduced) 561304-81-2 561353-88-6
RL: PRP (Properties)
(Unclaimed; **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)

IT 561347-54-4DP, **Albumin** (human), subfragments, **fusion** proteins 561347-55-5P 561347-56-6P 561347-57-7P 561347-58-8P
561347-59-9P 561347-60-2P 561347-61-3P 561347-62-4P 561347-63-5P
561347-64-6P 561347-65-7P 561347-66-8P 561347-67-9P 561347-68-0P
561347-69-1P 561347-70-4P 561347-71-5P 561347-72-6P 561347-73-7P
561347-74-8P 561347-75-9P 561347-76-0P 561347-77-1P 561347-78-2P
561347-79-3P
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)

IT 9004-10-8P, Insulin, biological studies 107444-51-9P, (7-36)Glucagon-like peptide 1 amide 141732-76-5P, Extendin 4
305835-60-3P, Bone morphogenetic protein 9
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)

IT 50-99-7, D-Glucose, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(maintenance of basel level of; human serum **albumin** **fusion** proteins for prolonged **shelf-life** of therapeutic proteins)

IT 561347-53-3
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(nucleotide sequence; human serum **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)

IT 561350-18-3, 1: PN: WO03059934 SEQID: 1 unclaimed DNA 561350-19-4, 2: PN: WO03059934 SEQID: 2 unclaimed DNA 561350-20-7, 5: PN: WO03059934 SEQID: 5 unclaimed DNA 561350-21-8, 6: PN: WO03059934 SEQID: 6 unclaimed DNA 561350-22-9, 7: PN: WO03059934 SEQID: 7 unclaimed DNA 561350-23-0, 8: PN: WO03059934 SEQID: 8 unclaimed DNA 561350-24-1, 9: PN: WO03059934 SEQID: 9 unclaimed DNA 561350-25-2 561350-26-3 561350-27-4
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561354-17-4 561354-18-5 561354-19-6 561354-20-9 561354-21-0
RL: PRP (Properties)
(unclaimed nucleotide sequence; **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)

IT 561354-22-1 561354-23-2 561354-24-3 561354-25-4 561354-26-5
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RL: PRP (Properties)
(unclaimed nucleotide sequence; **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)

IT 561350-49-0 561350-50-3 561350-51-4 561350-52-5 561350-53-6

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561350-69-4 561350-70-7 561350-71-8 561350-72-9 561350-73-0
561350-74-1 561350-75-2 561350-76-3 561350-77-4 561350-78-5
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561354-08-3 561354-09-4 561354-63-0 561354-64-1 561354-88-9
561354-89-0 561354-90-3 561354-91-4 561354-94-7 561354-95-8
RL: PRP (Properties)
(unclaimed protein sequence; **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)

IT 33017-11-7, Proinsulin C-peptide (human) 40958-31-4, Somatostatin (sheep reduced) 82177-09-1 85482-68-4 85734-71-0 122024-47-9
125677-89-6 130912-02-6 131748-18-0 131748-19-1 157654-59-6
166980-40-1 170098-75-6 192503-43-8 247166-37-6 367273-47-0
367273-48-1 477953-25-6 477953-26-7 477953-27-8 477953-28-9
477953-29-0 477953-30-3 477953-31-4 477953-32-5 477953-33-6
477953-34-7 477953-35-8 478188-11-3 478188-13-5 561304-79-8
561304-80-1 561304-82-3 561304-83-4 561304-84-5 561304-85-6
561304-86-7 561304-87-8 561304-88-9 561304-92-5 561304-95-8
RL: PRP (Properties)
(unclaimed sequence; **albumin fusion** proteins for prolonged **shelf-life** of therapeutic proteins)

L66 ANSWER 3 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:300832 HCAPLUS
DN 138:326508
ED Entered STN: 18 Apr 2003
TI **Albumin fusion** proteins with therapeutic proteins for improved **shelf-life**
IN **Rosen, Craig A.; Haseltine, William A.**
PA **Human Genome Sciences, Inc., USA**
SO PCT Int. Appl., 457 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K

CC 63-3 (Pharmaceuticals)
Section cross-reference(s): 3, 15
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003030821	A2	20030417	WO 2002-US31794	20021004
	WO 2003030821	A3	20031211		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-327281P P 20011005

AB The present invention encompasses **fusion** proteins of **albumin** with various therapeutic proteins. Therapeutic proteins may be stabilized to extend the **shelf-life**, and/or to retain the therapeutic protein's activity for extended periods of time in solution, in vitro and/or in vivo, by genetically or chemical **fusing** or conjugating the therapeutic protein to **albumin** or a fragment or variant of **albumin**. Use of **albumin fusion** proteins may also reduce the need to formulate the protein solns. with large excesses of carrier proteins to prevent loss of therapeutic proteins due to factors such as binding to the container. Nucleic acid mols. encoding the **albumin fusion** proteins of the invention are also encompassed by the invention, as are vectors containing these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the **albumin fusion** proteins of the invention and using these nucleic acids, vectors, and/or host cells. Thus, plasmid vectors are constructed in which DNA encoding the desired therapeutic protein may be inserted for expression of the **albumin fusion** proteins in yeast (pPPC0005) and mammalian cells (pC4:HSA). Yeast-derived signal sequences from Saccharomyces cerevisiae invertase SUC2 gene, or the stanniocalcin or native human serum **albumin** signal peptides, are used for secretion in yeast or mammalian systems, resp. Thus, the **fusion** product of human growth hormone with residues 1-387 of human serum **albumin** retains essentially intact biol. activity after 5 wk of incubation in tissue culture media at 37°, whereas **recombinant** human growth hormone used as control lost its biol. activity in the first week. Although the potency of the **albumin fusion** proteins is slightly lower than the unfused counterparts in rapid bioassays, their biol. stability results in much higher biol. activity in the longer term in vitro assay or in vivo assays. Addnl., the present invention encompasses pharmaceutical compns. Comprising **albumin fusion** proteins and methods of treating, preventing, or ameliorating diseases, disorders or conditions using **albumin fusion** proteins of the invention.

ST **albumin fusion** therapeutic protein **shelflife**

IT Drug delivery systems
Gene therapy
Human
Molecular cloning
(**albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT **Fusion proteins (chimeric proteins)**
Interferons
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(**albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Signal peptides
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Peptides, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(linkers; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Animal cell
(mammalian, **recombinant** expression host; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Plasmid vectors
(pC4:HSA, for mammalian cell expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Plasmid vectors
(pPPC0005, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Plasmid vectors
(pScCHSA, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Plasmid vectors
(pScNHSA, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Linking agents
(peptide; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Saccharomyces cerevisiae
Yeast
(**recombinant** expression host; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT **Albumins, biological studies**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(serum; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(signal sequence; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Antibodies
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(single chain; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(therapeutic; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT **Interferons**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(α ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 9002-72-6DP, Growth hormone, **fusion** proteins with **albumin**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 511566-72-6DP, **Albumin** (human blood serum), full-length or subfragment **fusion** proteins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 511566-73-7
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(nucleotide sequence; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 511603-12-6 511603-13-7 511603-14-8 511603-15-9 511603-16-0
511603-17-1 511603-18-2 511603-19-3 511603-20-6 511603-21-7
511603-22-8 511603-23-9 511603-24-0 511603-25-1 511603-26-2
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511603-57-9 511603-58-0 511603-59-1 511603-60-4 511603-61-5
511603-62-6 511603-63-7 511603-64-8 511603-65-9 511603-66-0
511603-67-1 511603-68-2 511603-69-3
RL: PRP (Properties)
(unclaimed nucleotide sequence; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 122024-47-9 131748-18-0 367273-46-9 367273-47-0 367273-48-1
RL: PRP (Properties)
(unclaimed sequence; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

L66 ANSWER 4 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:125793 HCAPLUS
DN 138:297265
ED Entered STN: 19 Feb 2003
TI An **IFN-β -Albumin Fusion** Protein That Displays Improved Pharmacokinetic and Pharmacodynamic Properties in Nonhuman Primates
AU Sung, Cynthia; Nardelli, Bernardetta; LaFleur, David W.; Blatter, Erich; Corcoran, Marta; Olsen, Henrik S.; Birse, Charles E.; Pickeral, Oxana K.; Zhang, Junli; Shah, Devanshi; Moody, Gordon; Gentz, Solange; Beebe, Lisa; Moore, Paul A.
CS **Human Genome Sciences, Inc., Rockville, MD, 20850, USA**
SO Journal of Interferon and Cytokine Research (2003), 23(1), 25-36
CODEN: JICRFJ; ISSN: 1079-9907
PB Mary Ann Liebert, Inc.
DT Journal
LA English
CC 1-7 (Pharmacology)
Section cross-reference(s): 15
AB The long half-life and stability of human serum **albumin** (HSA) make it an attractive candidate for **fusion** to short-lived therapeutic proteins. Albuferon beta (Human Genome Sciences [HGS], Inc., Rockville, MD) is a novel **recombinant** protein derived from a

gene **fusion** of **interferon-β** (**IFN-β**) and HSA. In vitro, Albuferon beta displays antiviral and antiproliferative activities and triggers the IFN-stimulated response element (ISRE) signal transduction pathway. Array anal. of 5694 independent genes in Daudi-treated cells revealed that Albuferon beta and **IFN-β** induce the expression of an identical set of 30 genes, including 9 previously not identified. In rhesus monkeys administered a dose of 50 μg/kg i.v. or s.c. or 300 μg/kg s.c., Albuferon beta demonstrated favorable pharmacokinetic properties. S.c. bioavailability was 87%, plasma clearance at 4.7-5.7 mL/h/kg was approx. 140-fold lower than that of **IFN-β** , and the terminal half-life was 36-40 h compared with 8 h for **IFN-beta.**. Importantly, Albuferon beta induced sustained increases in serum neopterin levels and 2',5'-oligoadenylate synthetase (2',5'-OAS) mRNA expression. At a molar dose equivalent to one-half the dose of **IFN-β** , Albuferon beta elicited comparable neopterin responses and significantly higher 2',5'-OAS mRNA levels in rhesus monkeys. The enhanced in vivo pharmacol. properties of **IFN-beta.** when **fused** to serum **albumin** suggest a clin. opportunity for improved **IFN-β** therapy.

ST **interferon beta albumin fusion** protein albuferon beta pharmacokinetic pharmacodynamic

IT **Fusion proteins (chimeric proteins)**
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**IFN-β** -HSA; **IFN-β** - **albumin fusion** protein with retained biol. activities and improved pharmacokinetic and pharmacodynamic properties of **IFN-β** in primates)

IT Antiviral agents
Human
Macaca mulatta
Pharmacodynamics
Pharmacokinetics
Signal transduction, biological
(**IFN-β** -**albumin fusion** protein with retained biol. activities and improved pharmacokinetic and pharmacodynamic properties of **IFN-β** in primates)

IT Genetic element
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ISRE (**interferon**-stimulated response element); **IFN -β** -**albumin fusion** protein with retained biol. activities and improved pharmacokinetic and pharmacodynamic properties of **IFN-β** in primates)

IT Transcriptional regulation
(activation; **IFN-β** -**albumin fusion** protein with retained biol. activities and improved pharmacokinetic and pharmacodynamic properties of **IFN-β** in primates)

IT Cell proliferation
(inhibition; **IFN-β** -**albumin fusion** protein with retained biol. activities and improved pharmacokinetic and pharmacodynamic properties of **IFN-β** in primates)

IT **Albumins, biological studies**
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(serum, human, **fusion** protein with **IFN-β** ; **IFN-β** -**albumin**

fusion protein with retained biol. activities and improved pharmacokinetic and pharmacodynamic properties of **IFN-β** in primates)

IT **Interferons**
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**β** , **fusion** protein with **albumin**; **IFN-β -albumin fusion** protein with retained biol. activities and improved pharmacokinetic and pharmacodynamic properties of **IFN-β** in primates)

IT 507485-69-0P, Albuferon **beta**
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**IFN-β** -HSA; **IFN-β** - **albumin fusion** protein with retained biol. activities and improved pharmacokinetic and pharmacodynamic properties of **IFN-β** in primates)

IT 2009-64-5, Neopterin 69106-44-1, 2',5'-Oligoadenylate synthetase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**IFN-β -albumin fusion** protein with retained biol. activities and improved pharmacokinetic and pharmacodynamic properties of **IFN-β** in primates)

RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L66 ANSWER 5 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:834389 HCAPLUS
DN 137:304506
ED Entered STN: 03 Nov 2002
TI Pharmacokinetic and pharmacodynamic studies of a human serum **albumin-interferon-α fusion** protein in cynomolgus monkeys
AU Osborn, Blaire L.; Olsen, Henrik S.; Nardelli, Bernardetta; Murray, James H.; Zhou, Joe X. H.; Garcia, Andrew; Moody, Gordon; Zaritskaya, Liubov S.; Sung, Cynthia
CS **Human Genome Sciences, Inc., Rockville, MD, USA**
SO Journal of Pharmacology and Experimental Therapeutics (2002), 303(2), 540-548
CODEN: JPETAB; ISSN: 0022-3565
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
CC 1-7 (Pharmacology)
Section cross-reference(s): 15
AB **Interferon-α (IFN-α)** is indicated for the treatment of certain viral **infections** including hepatitis B and C, and cancers such as melanoma. The short circulating half-life of unmodified **IFN-α** makes frequent dosing (daily or three times weekly) over an extended period (6-12 mo or more) necessary. To improve the pharmacokinetics of **IFN-α** and decrease dosing frequency, **IFN -α** was **fused** to human serum **albumin** producing a new protein, Albuferon. In vitro comparisons of Albuferon and **IFN-α** showed similar antiviral and antiproliferative activities, although Albuferon was less potent on a molar basis than **IFN-α** . Pharmacokinetic and pharmacodynamic properties of the **fusion** protein were enhanced in monkeys. After a single i.v. injection (30 μg/kg) clearance was 0.9 mL/h/kg, and the terminal half-life was 68 h. After 30 μg/kg s.c. injection, apparent clearance (clearance divided by bioavailability) was 1.4 mL/h/kg, the terminal half-life was 93 h, and bioavailability was 64%. The rate of clearance of Albuferon was approx. 140-fold slower, and the half-life 18-fold longer, than for **IFN-α** given by the s.c. route in other monkey studies. Sera from Albuferon-treated monkeys demonstrated dose-related antiviral activity for ≥8 days based on an in vitro bioassay, whereas antiviral activity from **IFN -α** -treated animals was only slightly elevated relative to vehicle on day 0. Significant increases in 2',5'-oligoadenylate synthetase mRNA relative to **IFN-α** - or vehicle-treated animals were maintained for ≥10 days after s.c. dosing. The improved pharmacokinetics of Albuferon are accompanied by an improved pharmacodynamic response suggesting that Albuferon may offer the benefits of less frequent dosing and a potentially improved efficacy profile compared with **IFN-α** .
ST Albuferon **interferon** antiviral antiproliferative pharmacokinetics pharmacodynamics
IT Antiviral agents
Cytotoxic agents
Human
Macaca irus

Pharmacodynamics
Pharmacokinetics
(pharmacokinetic and pharmacodynamic studies of a human serum **albumin-interferon-α fusion** protein in cynomolgus monkeys)

IT **Albumins, biological studies**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(serum, **fusion** protein with **interferon-α** ; pharmacokinetic and pharmacodynamic studies of a human serum **albumin-interferon-α** **fusion** protein in cynomolgus monkeys)

IT **Interferons**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α , **fusion** protein with human serum **albumin**; pharmacokinetic and pharmacodynamic studies of a human serum **albumin-interferon-α** **fusion** protein in cynomolgus monkeys)

IT 69106-44-1, 2',5'-Oligoadenylate synthetase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pharmacokinetic and pharmacodynamic studies of a human serum **albumin-interferon-α** **fusion** protein in cynomolgus monkeys)

IT 98530-12-2, Intron-A 472960-22-8, Albuferon
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacokinetic and pharmacodynamic studies of a human serum **albumin-interferon-α** **fusion** protein in cynomolgus monkeys)

RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L66 ANSWER 6 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:781112 HCAPLUS
DN 135:348852
ED Entered STN: 26 Oct 2001
TI **Albumin fusion** proteins with therapeutic proteins for improved **shelf-life**
IN **Rosen, Craig A.; Haseltine, William A.**
PA **Human Genome Sciences, Inc., USA**
SO PCT Int. Appl., 394 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N015-00
CC 63-3 (Pharmaceuticals)
Section cross-reference(s): 3, 15
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001079480	A1	20011025	WO 2001-US11991	20010412
	WO 2001079480	C2	20030109		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1276856	A1	20030122	EP 2001-937179	20010412
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2003125247	A1	20030703	US 2001-833041	20010412
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	JP 2003530852	T2	20031021	JP 2001-577463	20010412
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	WO 2001-US11991	W	20010412		

AB The present invention encompasses **fusion** proteins of **albumin** with various therapeutic proteins. Therapeutic proteins may be stabilized to extend the **shelf-life**, and/or to retain the therapeutic protein's activity for extended periods of time in solution, in vitro and/or in vivo, by genetically or chemical **fusing** or conjugating the therapeutic protein to **albumin** or a fragment or variant of **albumin**. Use of **albumin fusion** proteins may also reduce the need to formulate the protein solns. with large excesses of carrier proteins to prevent loss of therapeutic proteins due to factors such as binding to the container. Nucleic acid mols. encoding the **albumin fusion** proteins of the invention are also encompassed by the invention, as are vectors containing these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the **albumin fusion** proteins of the invention and using these nucleic acids, vectors, and/or host cells. Thus, plasmid vectors are constructed in which DNA encoding the desired

therapeutic protein may be inserted for expression of the **albumin fusion** proteins in yeast (pPPC0005) and mammalian cells (pC4:HSA). Yeast-derived signal sequences from Saccharomyces cerevisiae invertase SUC2 gene, or the stanniocalcin or native human serum **albumin** signal peptides, are used for secretion in yeast or mammalian systems, resp. Thus, the **fusion** product of human growth hormone with residues 1-387 of human serum **albumin** retains essentially intact biol. activity after 5 wk of incubation in tissue culture media at 37°, whereas **recombinant** human growth hormone used as control lost its biol. activity in the first week. Although the potency of the **albumin fusion** proteins is slightly lower than the unfused counterparts in rapid bioassays, their biol. stability results in much higher biol. activity in the longer term in vitro assay or in vivo assays. Addnl., the present invention encompasses pharmaceutical compns. comprising **albumin fusion** proteins and methods of treating, preventing, or ameliorating diseases, disorders or conditions using **albumin fusion** proteins of the invention.

ST **albumin fusion** therapeutic protein **shelflife**

IT Receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(4-1BB; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Cytokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(BAFF; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Cytokine receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(DR4 (death receptor 4); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Cytokine receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(DR5 (death receptor 5); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Cytokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MPIF-1 (myeloid progenitor inhibitory factor 1); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Steroid receptors
Thyroid hormone receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TR (thyroid/steroid hormone receptor), 11; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Steroid receptors
Thyroid hormone receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TR (thyroid/steroid hormone receptor), 12; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Steroid receptors
Thyroid hormone receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TR (thyroid/steroid hormone receptor), 13; **albumin**

fusion proteins with therapeutic proteins for improved **shelf-life**)

IT Steroid receptors
Thyroid hormone receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TR (thyroid/steroid hormone receptor), 14; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Steroid receptors
Thyroid hormone receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TR (thyroid/steroid hormone receptor), 16; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Steroid receptors
Thyroid hormone receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TR (thyroid/steroid hormone receptor), 8; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Steroid receptors
Thyroid hormone receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TR2 (thyroid/steroid hormone receptor 2); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Steroid receptors
Thyroid hormone receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TR3 (thyroid/steroid hormone receptor 3); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TRAIL (tumor necrosis factor-related apoptosis-inducing ligand); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Cytokine receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TRAIL, 4; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Cytokine receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TRAIL, 6; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Cytokine receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TRAIL-R3; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Drug delivery systems
Gene therapy
Molecular cloning
(**albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Cell adhesion molecules
Cytokines
Enzymes, biological studies
Fas antigen
Fas ligand
Fusion proteins (chimeric proteins)
Growth factors, animal
Interferons
Synthetic gene
Tumor necrosis factor receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(apoptosis-regulating, AIM-2; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Cytokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(endokine; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Signal peptides
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(for improved secretion in yeast or mammalian cells; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT **Interferons**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(keratinocyte-derived; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Animal cell
(mammalian, **recombinant** expression host; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Plasmid vectors
(pC4:HSA, for mammalian cell expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Plasmid vectors
(pPPC0005, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Plasmid vectors
(pScCHSa, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Plasmid vectors
(pScNHSA, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Saccharomyces cerevisiae
Yeast
(**recombinant** expression host; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT **Albumins, biological studies**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic

use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(serum; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(signal sequence, for improved secretion in yeast or mammalian cells; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Antibodies
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(single chain; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(therapeutic; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT **Interferons**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(α ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokine receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(β chemokine receptor CCR5; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Tumor necrosis factors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(γ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Tumor necrosis factors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(δ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 189460-40-0P, Connective tissue growth factor
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(2 and 4; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 9001-84-7P, Phospholipase A2
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(T-cell lymphoma lipoprotein-associated; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 9002-67-9P, Luteinizing hormone 9002-68-0P, FSH 9002-72-6P, Growth hormone 9004-10-8P, Insulin, biological studies 11096-26-7P, Erythropoietin 67763-96-6P, Insulin-like growth factor 1 83869-56-1P, GM-CSF 124861-55-8P, Proteinase inhibitor, **TIMP**-2 127464-60-2P, Vascular endothelial growth factor **140208-24-8P**, Proteinase inhibitor, **TIMP-1** 143011-72-7P, G-CSF 145809-21-8P, Proteinase inhibitor, **TIMP**-3 148348-15-6P, Fibroblast growth factor 7 171758-70-6P, Keratinocyte growth factor 2 186207-03-4P, Proteinase inhibitor, **TIMP**-4 205944-50-9P, Osteoprotegerin 207621-35-0P, Osteoprotegerin ligand 244019-42-9P, Vascular endothelial growth factor 2
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic

use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 127361-02-8DP, **Albumin** (human blood serum clone HSA-II/HSA-I-A protein moiety reduced), full-length or subfragment **fusion** products
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nucleotide sequence; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 155945-98-5, PN: US5962255 SEQID: 59 unclaimed DNA 156163-00-7 167728-69-0 167728-70-3 167728-71-4 167728-72-5 167728-73-6 167731-70-6 167731-74-0, PN: US5962255 SEQID: 56 unclaimed DNA 167731-75-1, PN: US5962255 SEQID: 57 unclaimed DNA 167731-76-2, PN: US5962255 SEQID: 58 unclaimed DNA 167731-77-3, PN: US5962255 SEQID: 60 unclaimed DNA 167731-78-4, PN: US5962255 SEQID: 61 unclaimed DNA 167731-79-5 167731-80-8 167731-81-9 167732-10-7 167732-11-8, PN: US5962255 SEQID: 551 unclaimed DNA 167732-12-9 167732-13-0 167732-14-1, PN: US5962255 SEQID: 554 unclaimed DNA 167732-15-2, PN: US5962255 SEQID: 555 unclaimed DNA 167732-16-3 167732-17-4 167732-18-5 167732-19-6, PN: US5962255 SEQID: 98 unclaimed DNA 167732-20-9, PN: US5962255 SEQID: 572 unclaimed DNA 167732-21-0 167732-22-1, PN: US5962255 SEQID: 574 unclaimed DNA 195164-37-5 217893-77-1, GenBank A63614 217893-78-2, GenBank A63615 217893-79-3, GenBank A63616 217893-80-6, GenBank A63617 217893-81-7, GenBank A63618 217893-82-8, GenBank A63619 217893-83-9, GenBank A63620 217893-84-0, GenBank A63621 217893-85-1, GenBank A63622 217893-86-2, GenBank A63624 217893-89-5, GenBank A63627 217893-90-8, GenBank A63628 217893-91-9, GenBank A63629 217893-92-0, GenBank A63630 367319-52-6 367319-53-7 367319-54-8 367319-55-9 367319-56-0 367319-57-1 367319-58-2 367319-59-3 367319-60-6 367319-61-7 367319-62-8 367319-63-9 367319-64-0 367319-65-1 367319-66-2
RL: PRP (Properties)
(unclaimed nucleotide sequence; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 173586-11-3 221879-28-3 222614-92-8 352583-76-7, Protein (human clone 785CIP2B_67) 370649-84-6 370649-85-7
RL: PRP (Properties)
(unclaimed protein sequence; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 122024-47-9 131748-18-0 244008-03-5, PN: WO9947540 SEQID: 3 unclaimed DNA 244008-06-8, PN: WO9947540 SEQID: 4 unclaimed DNA 244008-07-9, PN: WO9947540 SEQID: 5 unclaimed DNA 244008-08-0, PN: WO9947540 SEQID: 6 unclaimed DNA 244008-09-1, PN: WO9947540 SEQID: 7 unclaimed DNA 244008-12-6, 8: PN: WO0183510 SEQID: 8 unclaimed DNA 244008-13-7, PN: WO9947540 SEQID: 9 unclaimed DNA 244008-14-8, PN: WO9947540 SEQID: 10 unclaimed DNA 367273-46-9 367273-47-0 367273-48-1 370598-71-3 370649-86-8
RL: PRP (Properties)
(unclaimed sequence; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Delta Biotechnology Limited; EP 0322094 A1 1989 HCAPLUS
(2) Delta Biotechnology Limited; WO 9523857 A1 1995 HCAPLUS

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TI **Albumin fusion** proteins with therapeutic proteins for

improved **shelf-life**
IN **Rosen, Craig A.; Haseltine, William A.**
PA **Human Genome Sciences, Inc, USA**
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PI	WO 2001079444	A2	20011025	WO 2001-US12013	20010412
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 2001074809	A5	20011020	AU 2001-74809	20010412
	EP 1278544	A2	20030129	EP 2001-941457	20010412
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2003125247	A1	20030703	US 2001-833041	20010412
	US 2003171267	A1	20030911	US 2001-833117	20010412
	JP 2003530847	T2	20031021	JP 2001-577428	20010412
	US 2003199043	A1	20031023	US 2001-832501	20010412
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PRAI	US 2000-229358P	P	20000412		
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	US 2000-256931P	P	20001221		
	WO 2001-US12013	W	20010412		

AB The present invention encompasses **fusion** proteins of **albumin** with various therapeutic proteins. Therapeutic proteins may be stabilized to extend the **shelf-life**, and/or to retain the therapeutic protein's activity for extended periods of time in solution, in vitro and/or in vivo, by genetically or chemical **fusing** or conjugating the therapeutic protein to **albumin** or a fragment or variant of **albumin**. Use of **albumin fusion** proteins may also reduce the need to formulate the protein solns. with large excesses of carrier proteins to prevent loss of therapeutic proteins due to factors such as binding to the container. Nucleic acid mols. encoding the **albumin fusion** proteins of the invention are also encompassed by the invention, as are vectors containing these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the **albumin fusion** proteins of the invention and using these nucleic acids, vectors, and/or host cells. Thus, plasmid vectors are constructed in which DNA encoding the desired therapeutic protein may be inserted for expression of the **albumin fusion** proteins in yeast (pPPC0005) and mammalian cells (pC4:HSA). Yeast-derived signal sequences from Saccharomyces cerevisiae invertase SUC2 gene, or the stanniocalcin or native human serum **albumin** signal peptides, are used for secretion in yeast or mammalian systems, resp. Thus, the **fusion** product of human growth hormone with residues 1-387 of human serum **albumin** retains essentially intact biol. activity after 5 wk of incubation in tissue culture media at 37°, whereas **recombinant** human growth hormone used as

control lost its biol. activity in the first week. Although the potency of the **albumin fusion** proteins is slightly lower than the unfused counterparts in rapid bioassays, their biol. stability results in much higher biol. activity in the longer term in vitro assay or in vivo assays. Addnl., the present invention encompasses pharmaceutical compns. comprising **albumin fusion** proteins and methods of treating, preventing, or ameliorating diseases, disorders or conditions using **albumin fusion** proteins of the invention.

ST **albumin fusion** therapeutic protein **shelflife**

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(1-309; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Bone morphogenetic proteins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(11; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Bone morphogenetic proteins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(12; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Bone morphogenetic proteins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(15; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Bone morphogenetic proteins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(17; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Bone morphogenetic proteins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(18; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Interleukins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(19; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Bone morphogenetic proteins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(1; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Interleukins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(21; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Bone morphogenetic proteins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(2; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(331D5; **albumin fusion** proteins with therapeutic

proteins for improved **shelf-life**)

IT Bone morphogenetic proteins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(3; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(4-1BB; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Bone morphogenetic proteins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(4; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Bone morphogenetic proteins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(5; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(61164; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Bone morphogenetic proteins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(6; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Bone morphogenetic proteins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(7; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Bone morphogenetic proteins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(9; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Platelet-derived growth factors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(AA; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(ACRP-30; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(ADEC (adenoid expressed chemokine); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Interleukins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(AGF; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class

RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(APM-1; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Act-2; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Platelet-derived growth factors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(BB; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(BCMA; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Platelet-derived growth factors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Bv-sis; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(C-C, 2; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(C-C, 3; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(C-C, DGWCC; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(C-C, DVic-1; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(C-C, ELC; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(C-C, HCC-1; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(C-C, IBICK; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(C-C, ILINCK; **albumin fusion** proteins with

therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(C-C, SLC (secondary lymphoid chemokine); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(C-C, STCP-1; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(C-X-C, 3; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(C-X-C; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(C10; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Troponins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(C; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CCC3; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CCF18; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CCR2; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT CD antigens
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CD27; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Glycoproteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CD40-L (antigen CD40 ligand); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CTAP-III (connective tissue activating protein III); **albumin fusion** proteins with therapeutic proteins for improved

shelf-life)

IT Antigens
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CTLA-8; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokine receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(CXCR3; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Cerebus; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Chr19Kine; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Platelet-derived growth factors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(D; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Cytokine receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(DR3 (death receptor 3); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(EDAR; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Interleukins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(EDIRF I protein; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(EEC (eosinophil expressed chemokine); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(ENA-78 (epithelial neutrophil activating protein-78); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Hemopoietins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(FLT3 ligand; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HCC-1; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Troponins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(I; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(L105-7; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(LVEC-1 (liver expressed chemokine 1); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(LVEC-2 (liver expressed chemokine 2); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Lyn-1; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(M110; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(M11A; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MACK (mammary associated chemokine); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MCP-3α and MCP-3β; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MCP-4; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MCPP (monocyte chemotactic proprotein); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(MDC (macrophage-derived chemokine); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Monokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MIG (monokine induced by γ- **interferon**); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MIG-β; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Interleukins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MIRAP; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MP52; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(NOGO-66; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(NOGO-A; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(NOGO-B; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(NOGO-C; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Antigens
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(OX-40; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(PF4; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(PGBC (pituitary expressed chemokine); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokine receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(RANTES; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(SISD; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(SLC (secondary lymphoid tissue chemokine); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Troponins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(T; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TAC1; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Cytokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TARC (thymus and activation regulated cytokine); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TMEC (T cell mixed lymphocyte reaction expressed chemokine); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Tarc; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Tim-1; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Troy; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(ZCHEMO-8; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(ZSIG-35; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Drug delivery systems
Gene therapy
Molecular cloning

(**albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT CD30 (antigen)
CD40 (antigen)
Cell adhesion molecules
Cytokines
Enzymes, biological studies
Eotaxin
Erythropoietin receptors
Fas ligand
Fusion proteins (chimeric proteins)
Granulocyte-macrophage colony-stimulating factor receptors
Growth factors, animal
Interferons
Interleukin 1
Interleukin 1 receptor antagonist
Interleukin 11
Interleukin 13
Interleukin 14
Interleukin 15
Interleukin 17
Interleukin 18
Interleukin 1α
Interleukin 1β
Interleukin 3
Interleukin 4
Interleukin 4 receptors
Interleukin 5 receptors
Interleukin 6
Interleukin 6 receptors
Interleukin 8
Interleukin 8 receptors
Interleukin 9
Lymphotoxin
Monocyte chemoattractant protein-1
Neutrophil-activating peptide-2
Platelet-derived growth factors
RANTES (chemokine)
Stem cell factor
Synthetic gene
Tumor necrosis factor receptors
Tumor necrosis factors
Vascular endothelial growth factor receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Interleukin 10
Interleukin 12
Interleukin 2
Interleukin 5
Interleukin 7
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(b57; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(chemokine-like protein PF4-414; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Growth factors, animal
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(chondromodulins, -like protein; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(collapsins, antibodies for; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(exodus; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Signal peptides
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(for improved secretion in yeast or mammalian cells; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(fractalkines; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Agglutinins and Lectins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(galectin-4; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(gene Patched-2; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Vascular endothelial growth factor receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(gene flt 1; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Vascular endothelial growth factor receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(gene flt 4; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(gene patched; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(glycodelin-A; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(granulocyte chemotactic protein-2; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(gro-α; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(gro-β; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(gro-γ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(growth-related oncogene-α; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(growth-related oncogene-β; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(growth-related oncogene-γ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Cytokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**interferon**-inducible IP-10; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Interleukin receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(interleukin 10 receptors; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Interleukin receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(interleukin 11; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Interleukin receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(interleukin 12; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Interleukin receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(interleukin 13; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Interleukin receptors

RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(interleukin 15; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Interleukin receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(interleukin 17; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Interleukin receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(interleukin 9; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(interleukin C; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(interleukin-1 accessory; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(interleukin-2 receptor associated p43; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Lymphokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(lymphotactins; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(macrophage **inflammatory** protein 3α; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(macrophage **inflammatory** protein 3β; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(macrophage **inflammatory** protein 3γ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Animal cell
(mammalian, **recombinant** expression host; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Antitumor agents
(melanoma; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(monocyte chemoattractant protein 3; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokine receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monocyte chemoattractant protein-1; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monocyte chemoattractant protein-2; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokine receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monocyte chemoattractant protein-4; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(neurotactin; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Growth factors, animal
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(osteogenic protein 2; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Tumor necrosis factor receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(p75; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Plasmid vectors
(pC4:HSA, for mammalian cell expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Plasmid vectors
(pPPC0005, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Plasmid vectors
(pScCHSa, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Plasmid vectors
(pScNHSA, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Placental hormones
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(placenta-derived mitogenic factors; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Saccharomyces cerevisiae
Yeast
(**recombinant** expression host; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT **Albumins, biological studies**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(serum; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(signal sequence, for improved secretion in yeast or mammalian cells; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Antibodies
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(single chain; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(stem cell inhibitory factor; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Growth factors, animal
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(stroma-derived growth factor 1α and 1β; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(therapeutic; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Interleukin 1 receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(type 3; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Interleukin 1 receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(type II; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT **Interferons**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(α ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokine receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(β chemokine receptor CCR5; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokine receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(β chemokine receptor CCR7; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Transforming growth factors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(β1-; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Transforming growth factors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(β2-; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokines
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(β9; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Thrombomodulin
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(β; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 78990-62-2P, Calpain
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(10a and 10b and 10c; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 50-56-6P, Oxytocin, biological studies 9002-62-4P, Prolactin, biological studies 9002-67-9P, Luteinizing hormone 9002-68-0P, FSH 9002-72-6P, Growth hormone 9004-10-8P, Insulin, biological studies 9014-42-0P, Thrombopoietin 11000-17-2P, Vasopressin 11096-26-7P, Erythropoietin 33507-63-0P, Substance P 67763-96-6P, Insulin-like growth factor 1 83869-56-1P, GM-CSF 106096-92-8P, Acidic fibroblast growth factor 106096-93-9P, Basic fibroblast growth factor 122191-40-6P, ICE proteinase 123584-45-2P, Fibroblast growth factor 4 129653-64-1P, Fibroblast growth factor 5 130939-41-2P, Fibroblast growth factor 6 130939-66-1P, Neurotrophin 3 140208-23-7P, Plasminogen activator inhibitor-1 141760-45-4P, Furin 142243-03-6P, Plasminogen activator inhibitor-2 143011-72-7P, G-CSF 143375-33-1P, Neurotrophin 4 148348-14-5P, Fibroblast growth factor 3 151185-16-9P, Fibroblast growth factor 9 157857-21-1P, Maspin 164003-41-2P, Fibroblast growth factor 8 185915-22-4P, Fibroblast growth factor 13 187888-07-9P, Endostatin 193363-12-1P, Vascular endothelial growth factor D 203874-76-4P, Fibroblast growth factor 12 204719-95-9P, Fibroblast growth factor 16 214210-47-6P, Neuropilin 1 219563-02-7P, Vascular endothelial growth factor E 227018-38-4P, Neuropilin 2 271597-10-5P, Growth/differentiation factor 1 322637-18-3P, Fibroblast growth factor 18 331718-56-0P, Resistin 332350-92-2P, Bone morphogenetic protein receptor kinase 3
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 144114-21-6, Retropepsin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 127464-60-2P, Vascular endothelial growth factor
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(isoforms; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 127361-02-8DP, **Albumin** (human blood serum clone HSA-II/HSA-I-A protein moiety reduced), full-length or subfragment **fusion** products
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nucleotide sequence; **albumin fusion** proteins with

therapeutic proteins for improved **shelf-life**)

IT 155945-98-5, PN: US5962255 SEQID: 59 unclaimed DNA 156163-00-7 167728-69-0 167728-70-3 167728-71-4 167728-72-5 167728-73-6 167731-70-6 167731-74-0, PN: US5962255 SEQID: 56 unclaimed DNA 167731-75-1, PN: US5962255 SEQID: 57 unclaimed DNA 167731-76-2, PN: US5962255 SEQID: 58 unclaimed DNA 167731-77-3, PN: US5962255 SEQID: 60 unclaimed DNA 167731-78-4, PN: US5962255 SEQID: 61 unclaimed DNA 167731-79-5 167731-80-8 167731-81-9 167732-10-7 167732-11-8, PN: US5962255 SEQID: 551 unclaimed DNA 167732-12-9 167732-13-0 167732-14-1, PN: US5962255 SEQID: 554 unclaimed DNA 167732-15-2, PN: US5962255 SEQID: 555 unclaimed DNA 167732-16-3 167732-17-4 167732-18-5 167732-19-6, PN: US5962255 SEQID: 98 unclaimed DNA 167732-20-9, PN: US5962255 SEQID: 572 unclaimed DNA 167732-21-0 167732-22-1, PN: US5962255 SEQID: 574 unclaimed DNA 195164-37-5 217893-77-1, GenBank A63614 217893-78-2, GenBank A63615 217893-79-3, GenBank A63616 217893-80-6, GenBank A63617 217893-81-7, GenBank A63618 217893-82-8, GenBank A63619 217893-83-9, GenBank A63620 217893-84-0, GenBank A63621 217893-85-1, GenBank A63622 217893-86-2, GenBank A63624 217893-89-5, GenBank A63627 217893-90-8, GenBank A63628 217893-91-9, GenBank A63629 217893-92-0, GenBank A63630 244008-03-5, PN: WO9947540 SEQID: 3 unclaimed DNA 367319-52-6 367319-53-7 367319-54-8 367319-55-9 367319-56-0 367319-57-1 367319-58-2 367319-59-3 367319-60-6 367319-61-7 367319-62-8 367319-63-9 367319-64-0 367319-65-1 367319-66-2 370965-07-4 370965-08-5
RL: PRP (Properties)
(unclaimed nucleotide sequence; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 122024-47-9 131748-18-0 244008-06-8, PN: WO9947540 SEQID: 4 unclaimed DNA 244008-07-9, PN: WO9947540 SEQID: 5 unclaimed DNA 244008-08-0, PN: WO9947540 SEQID: 6 unclaimed DNA 244008-09-1, PN: WO9947540 SEQID: 7 unclaimed DNA 244008-12-6, 8: PN: WO0183510 SEQID: 8 unclaimed DNA 244008-13-7, PN: WO9947540 SEQID: 9 unclaimed DNA 367273-46-9 367273-47-0 367273-48-1 371149-71-2
RL: PRP (Properties)
(unclaimed sequence; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 102510-92-9P, Inhibin A
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(α- and β-subunits; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 9061-61-4P, Nerve growth factor
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(β; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

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IN **Rosen, Craig A.; Haseltine, William A.**
PA **Human Genome Sciences, Inc., USA**
SO PCT Int. Appl., 374 pp.
CODEN: PIXXD2
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LA English
IC ICM C12N
CC 63-3 (Pharmaceuticals)

Section cross-reference(s): 3, 15

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	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001079443	A2	20011025	WO 2001-US11924	20010412
	WO 2001079443	A3	20020221		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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	AU 2001059063	A5	20011030	AU 2001-59063	20010412
	EP 1274719	A2	20030115	EP 2001-932546	20010412
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2003125247	A1	20030703	US 2001-833041	20010412
	US 2003171267	A1	20030911	US 2001-833117	20010412
	JP 2003530846	T2	20031021	JP 2001-577427	20010412
	US 2003199043	A1	20031023	US 2001-832501	20010412
	US 2003219875	A1	20031127	US 2001-833118	20010412
	US 2004010134	A1	20040115	US 2001-833245	20010412
PRAI	US 2000-229358P	P	20000412		
	US 2000-199384P	P	20000425		
	US 2000-256931P	P	20001221		
	WO 2001-US11924	W	20010412		

AB The present invention encompasses **fusion** proteins of **albumin** with various therapeutic proteins. Therapeutic proteins may be stabilized to extend the **shelf-life**, and/or to retain the therapeutic protein's activity for extended periods of time in solution, in vitro and/or in vivo, by genetically or chemical **fusing** or conjugating the therapeutic protein to **albumin** or a fragment or variant of **albumin**. Use of **albumin fusion** proteins may also reduce the need to formulate the protein solns. with large excesses of carrier proteins to prevent loss of therapeutic proteins due to factors such as binding to the container. Nucleic acid mols. encoding the **albumin fusion** proteins of the invention are also encompassed by the invention, as are vectors containing these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the **albumin fusion** proteins of the invention and using these nucleic acids, vectors, and/or host cells. Thus, plasmid vectors are constructed in which DNA encoding the desired therapeutic protein may be inserted for expression of the **albumin fusion** proteins in yeast (pPPC0005) and mammalian cells (pC4:HSA). Yeast-derived signal sequences from Saccharomyces cerevisiae invertase SUC2 gene, or the stanniocalcin or native human serum **albumin** signal peptides, are used for secretion in yeast or mammalian systems, resp. Thus, the **fusion** product of human growth hormone with residues 1-387 of human serum **albumin** retains essentially intact biol. activity after 5 wk of incubation in tissue culture media at 37°, whereas **recombinant** human growth hormone used as control lost its biol. activity in the first week. Although the potency of the **albumin fusion** proteins is slightly lower than the unfused counterparts in rapid bioassays, their biol. stability results in much higher biol. activity in the longer term in vitro assay or in vivo assays. Addnl., the present invention encompasses pharmaceutical compns. comprising **albumin fusion** proteins and methods of treating, preventing, or ameliorating diseases, disorders or conditions using **albumin fusion** proteins of the invention.

ST **albumin fusion** therapeutic protein **shelflife**

IT Bone morphogenetic proteins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(2; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Bone morphogenetic proteins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(7; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Transport proteins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(ABC1 (ATP-binding cassette-containing 1); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(ADMP (anti-dorsalizing morphogenetic protein-1); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Agouti signal; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(BPI (bactericidal/permeability-increasing), 21; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Transcription factors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(BRCA1; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Transcription factors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(BRCA2; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Del-1 (developmentally regulated endothelial locus-1); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(EMAP II (endothelial monocyte activating polypeptide II); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Troponins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(I; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Toxins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(ML-I (mistletoe lectin I); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MTP (microsomal transfer protein); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(NIF (neutrophil inhibitory factor); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(T1/ST2; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Glycoproteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TNF-BP (tumor necrosis factor-binding protein); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(TRAIL (tumor necrosis factor-related apoptosis-inducing ligand); **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Drug delivery systems
Gene therapy
Molecular cloning
(**albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Arrestins
CD4 (antigen)
CTLA-4 (antigen)
Calreticulin
Cell adhesion molecules
Ciliary **neurotrophic** factor
Cytokines
Decorins
Enzymes, biological studies
Fusion proteins (chimeric proteins)
Gelsolin
Growth factors, animal
Heat-shock proteins
Interferons
Interleukin 1
Interleukin 1 receptor antagonist
Interleukin 10
Interleukin 11
Interleukin 12
Interleukin 18
Interleukin 4
Interleukin 4 receptors
Interleukin 8
LFA-3 (antigen)
Lactoferrins
Leukemia inhibitory factor
Myelin basic protein

Platelet-derived growth factors
Pleiotrophins
Stem cell factor
Synthetic gene
Tumor necrosis factor receptors
Tumor necrosis factor receptors
Tumor necrosis factors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT **Neurotrophic factors**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**brain-derived; albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(chemokine-binding; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(corticotropin-releasing factor-binding; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Toxins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(diphtheria, **fusion** protein with interleukin 2; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Toxins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(exotoxins, Pseudomonas, **fusion** protein with acidic fibroblast growth factor; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Signal peptides
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(for improved secretion in yeast or mammalian cells; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Interleukin 3
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**fusion** protein with G-CSF; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Interleukin 6
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**fusion** proteins with diphtheria toxin or Pseudomonas exotoxin; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(gene patched; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT **Neurotrophic** factors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(glial-derived; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT **Interferons**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**interferon** ω; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**interferon**-induced, 10; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Animal cell
(mammalian, **recombinant** expression host; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(noggins; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Plasmid vectors
(pC4:HSA, for mammalian cell expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Plasmid vectors
(pPPC0005, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Plasmid vectors
(pScCHSa, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Plasmid vectors
(pScNHSA, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Hemopoietins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(progenipoietin; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Hemopoietins
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(promegapoietin; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Saccharomyces cerevisiae
Yeast
(**recombinant** expression host; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Antigens
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(retinal S-; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT **Albumins, biological studies**

RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(serum; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(signal sequence, for improved secretion in yeast or mammalian cells; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Antibodies
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(single chain; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Hedgehog protein
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(sonic; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(therapeutic; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tie-2; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Complement receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(type 1; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Collagens, biological studies
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(type II; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT **Interferons**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(τ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT **Interferons**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(α ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Transforming growth factors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(β1-; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Transforming growth factors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(β2-; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Transforming growth factors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(β3-; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT **Interferons**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(γ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 139691-92-2P, Serine proteinase inhibitor
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(1; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 9001-91-6DP, Lys-plasminogen, de-(1-76) derivs.
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Lys-plasminogen; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 9001-42-7P, α-Glucosidase 9002-01-1P, Streptokinase 9002-12-4P, Urate oxidase 9002-61-3P, Chorionic gonadotropin 9002-67-9P, Luteinizing hormone 9002-68-0P, FSH 9002-69-1P, Relaxin 9002-72-6P, Growth hormone 9003-98-9P, DNase 9004-10-8P, Insulin, biological studies 9007-92-5P, Glucagon, biological studies 9014-42-0P, Thrombopoietin 9015-68-3P, Asparaginase 9025-35-8P, α-Galactosidase 9026-93-1P, Adenosine deaminase 9035-55-6P, Adiposin 9039-53-6P, Urokinase 9040-61-3P, Staphylokinase 9054-89-1DP, Superoxide dismutase, **fusion** protein with botulin 9061-61-4P, Nerve growth factor 9073-56-7P, α-L-Iduronidase 9088-41-9P, Kunitz proteinase inhibitor 11096-26-7P, Erythropoietin 37228-64-1P, β-Glucocerebrosidase 42616-25-1P, Methioninase 55354-43-3P, Arylsulfatase B 62229-50-9P, Epidermal growth factor 67763-96-6P, Insulin-like growth factor 1 76901-00-3P, Platelet activating factor acetylhydrolase 82707-54-8P, Neprilysin 83652-28-2P, Calcitonin gene-related peptide 83869-56-1P, GM-CSF 86090-08-6P, Angiostatin 99149-95-8P, Saruplase 104625-48-1P, Activin A 105844-41-5P, Plasminogen activator inhibitor 106096-92-8DP, Acidic fibroblast growth factor, **fusion** protein with Pseudomonas exotoxin 106096-92-8P 106096-93-9P, Fibroblast growth factor 2 107231-12-9DP, Botulin, **fusion** protein with superoxide dismutase 116036-70-5P, Fibrolase 130939-66-1P, Neurotrophin 3 139639-23-9P, Tissue-type plasminogen activator 143011-72-7P, G-CSF 145137-38-8P, Desmoteplase 153858-68-5P, Contortrostatin 157857-21-1P, Maspin 163658-39-7P, Prosaptide 169494-85-3P, Leptin 186270-49-5P, Angiopoietin 1 194368-66-6P, Angiopoietin 2 194554-71-7P, Tissue factor pathway inhibitor 195009-21-3P, Glial growth factor 2 196488-72-9P, Ranpirnase 197980-93-1P, Pigment epithelium-derived factor 205944-50-9P, Osteoprotegerin 244019-30-5P, Vascular endothelial growth factor 1 320336-96-7P, Kistrin 362605-29-6P, Keratinocyte growth factor 1
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 9000-95-7P, Apyrase
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(ecto-; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 9002-79-3P, MSH
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**fusion** products with diphtheria toxin; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 127361-02-8DP, **Albumin** (human blood serum clone HSA-II/HSA-I-A protein moiety reduced), full-length or subfragment **fusion** products
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nucleotide sequence; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 131748-18-0 156163-00-7 217893-77-1, GenBank A63614 217893-78-2, GenBank A63615 217893-79-3, GenBank A63616 217893-80-6, GenBank A63617 217893-81-7, GenBank A63618 217893-82-8, GenBank A63619 217893-83-9, GenBank A63620 217893-84-0, GenBank A63621 217893-85-1, GenBank A63622 217893-86-2, GenBank A63624 217893-89-5, GenBank A63627 217893-90-8, GenBank A63628 217893-91-9, GenBank A63629 217893-92-0, GenBank A63630 367319-52-6 367319-53-7 367319-54-8 367319-55-9 367319-56-0 367319-58-2 367319-59-3 367319-60-6 367319-61-7 367319-62-8 367319-63-9 367319-64-0 367319-65-1 367319-66-2
RL: PRP (Properties)
(unclaimed nucleotide sequence; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 229477-44-5 244008-03-5, PN: WO9947540 SEQID: 3 unclaimed DNA 244008-06-8, PN: WO9947540 SEQID: 4 unclaimed DNA 244008-07-9, PN: WO9947540 SEQID: 5 unclaimed DNA 244008-08-0, PN: WO9947540 SEQID: 6 unclaimed DNA 244008-09-1, PN: WO9947540 SEQID: 7 unclaimed DNA 244008-12-6, 8: PN: WO0183510 SEQID: 8 unclaimed DNA 244008-13-7, PN: WO9947540 SEQID: 9 unclaimed DNA 244008-14-8, PN: WO9947540 SEQID: 10 unclaimed DNA 367273-46-9 367273-47-0 367273-48-1 370571-84-9
RL: PRP (Properties)
(unclaimed sequence; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 114949-22-3P, Activin
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(βc; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

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AN 2001:781077 HCAPLUS
DN 135:348849
ED Entered STN: 26 Oct 2001
TI **Albumin fusion** proteins with therapeutic proteins for improved **shelf-life**
IN **Rosen, Craig A.; Haseltine, William A.**
PA **Human Genome Sciences, Inc., USA**
SO PCT Int. Appl., 413 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N
CC 63-3 (Pharmaceuticals)
Section cross-reference(s): 3, 15
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PI	WO 2001079442	A2	20011025	WO 2001-US11850	20010412
	WO 2001079442	A3	20020606		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 2001064563 A5 20011030 AU 2001-64563 20010412
EP 1276849 A2 20030122 EP 2001-938994 20010412
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
US 2003125247 A1 20030703 US 2001-833041 20010412
US 2003171267 A1 20030911 US 2001-833117 20010412
US 2003199043 A1 20031023 US 2001-832501 20010412
JP 2003531590 T2 20031028 JP 2001-577426 20010412
US 2003219875 A1 20031127 US 2001-833118 20010412
US 2004010134 A1 20040115 US 2001-833245 20010412
PRAI US 2000-229358P P 20000412
US 2000-199384P P 20000425
US 2000-256931P P 20001221
WO 2001-US11850 W 20010412

AB The present invention encompasses **fusion** proteins of **albumin** with various therapeutic proteins, and in particular various antibodies. Therapeutic proteins may be stabilized to extend the **shelf-life**, and/or to retain the therapeutic protein's activity for extended periods of time in solution, in vitro and/or in vivo, by genetically or chemical **fusing** or conjugating the therapeutic protein to **albumin** or a fragment or variant of **albumin** . Use of **albumin fusion** proteins may also reduce the need to formulate the protein solns. with large excesses of carrier proteins to prevent loss of therapeutic proteins due to factors such as binding to the container. Nucleic acid mols. encoding the **albumin fusion** proteins of the invention are also encompassed by the invention, as are vectors containing these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the **albumin fusion** proteins of the invention and using these nucleic acids, vectors, and/or host cells. Thus, plasmid vectors are constructed in which DNA encoding the desired therapeutic protein may be inserted for expression of the **albumin fusion** proteins in yeast (pPPC0005) and mammalian cells (pC4:HSA). Yeast-derived signal sequences from Saccharomyces cerevisiae invertase SUC2 gene, or the stanniocalcin or native human serum **albumin** signal peptides, are used for secretion in yeast or mammalian systems, resp. Thus, the **fusion** product of human growth hormone with residues 1-387 of human serum **albumin** retains essentially intact biol. activity after 5 wk of incubation in tissue culture media at 37°, whereas **recombinant** human growth hormone used as control lost its biol. activity in the first week. Although the potency of the **albumin fusion** proteins is slightly lower than the unfused counterparts in rapid bioassays, their biol. stability results in much higher biol. activity in the longer term in vitro assay or in vivo assays. Addnl., the present invention encompasses pharmaceutical compns. comprising **albumin fusion** proteins and methods of treating, preventing, or ameliorating diseases, disorders or conditions using **albumin fusion** proteins of the invention.

ST **albumin fusion** therapeutic protein **shelflife**

IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(17-1A, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(B7.2, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CA125, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT CD antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study) (CD147, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
IT CD antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study) (CD33, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
IT CD antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study) (CD48, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
IT CD antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study) (CD52, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
IT CD antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study) (CD6, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
IT Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (E, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study) (HLA-DR, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study) (HM1.24, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
IT Cell adhesion molecules
RL: BSU (Biological study, unclassified); BIOL (Biological study) (ICAM-1 (intercellular adhesion mol. 1), antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
IT Immunoglobulin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (IgG type I, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
IT Selectins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (L-, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (LPAM-1 (lymphocyte Peyer's patch high endothelial venule adhesion mol. 1), antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
IT Blood-group substances
RL: BSU (Biological study, unclassified); BIOL (Biological study) (Lex, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
IT Blood-group substances
RL: BSU (Biological study, unclassified); BIOL (Biological study) (Ley, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
IT Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (M, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
IT Histocompatibility antigens

RL: BSU (Biological study, unclassified); BIOL (Biological study) (MHC (major histocompatibility complex), class I, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study) (MHC (major histocompatibility complex), class II, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study) (NogoA, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study) (Nsf2, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Glycoproteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study) (P170, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Cell adhesion molecules
RL: BSU (Biological study, unclassified); BIOL (Biological study) (SC-1, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study) (SF-25, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study) (SSEA-1 (stage-specific embryonic antigen 1), antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study) (TAG-72 (tumor-associated glycoprotein 72), antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Cell adhesion molecules
RL: BSU (Biological study, unclassified); BIOL (Biological study) (VCAM-1, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Drug delivery systems
Gene therapy
Molecular cloning
(**albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Antibodies
Cell adhesion molecules
Cytokines
Enzymes, biological studies
Fusion proteins (chimeric proteins)
Growth factors, animal
Immunoglobulins
Interferons
Synthetic gene
Tumor necrosis factor receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Angiogenic factors

CD14 (antigen)
CD2 (antigen)
CD20 (antigen)
CD22 (antigen)
CD3 (antigen)
CD30 (antigen)
CD38 (antigen)
CD4 (antigen)
CD40 (antigen)
CD44 (antigen)
CD45 (antigen)
CD5 (antigen)
CD8 (antigen)
CD80 (antigen)
CD80 (antigen)
CTLA-4 (antigen)
Carcinoembryonic antigen
Epidermal growth factor receptors
Fas antigen
Integrins
Interleukin 4 receptors
Interleukin 5
LFA-1 (antigen)
Mucins
TCR (T cell receptors)
Transferrin receptors
neu (receptor)
RL: BSU (Biological study, unclassified); BIOL (Biological study) (antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Mucins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (episialins, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Signal peptides
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(for improved secretion in yeast or mammalian cells; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Glycoproteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study) (gD, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Envelope proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (gp120env, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Glycoproteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study) (gpII, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Animal cell
(mammalian, **recombinant** expression host; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Agglutinins and Lectins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (mannan-binding, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Antibodies
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic

use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monoclonal; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Plasmid vectors
(pC4:HSA, for mammalian cell expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Plasmid vectors
(pPPC0005, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Plasmid vectors
(pScCHSa, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Plasmid vectors
(pScNHSA, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Interleukin 6 receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(receptor-associated glycoprotein gp130, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Saccharomyces cerevisiae
Yeast
(**recombinant** expression host; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT **Albumins, biological studies**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(serum; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(signal sequence, for improved secretion in yeast or mammalian cells; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Antibodies
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(single chain; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Venoms
(snake, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(therapeutic; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Globulins, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(thymocyte, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(tumor-associated, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Interleukin 2 receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α-chain, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT **Interferons**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(α ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(αIIbβ3, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Vitronectin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(αvβ3, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α4β1, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Chemokine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β chemokine receptor CCR5, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β2, antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 9002-67-9P, Luteinizing hormone 9002-68-0P, FSH 9002-72-6P, Growth hormone 9004-10-8P, Insulin, biological studies 11096-26-7P, Erythropoietin 67763-96-6P, Insulin-like growth factor 1 83869-56-1P, GM-CSF 143011-72-7P, G-CSF
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 156586-89-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 11016-39-0, Properdin 19600-01-2, Ganglioside GM2 20830-75-5, Digoxin 99085-47-9, CD55 antigen
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antibodies to; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 127361-02-8DP, **Albumin** (human blood serum clone HSA-II/HSA-I-A protein moiety reduced), full-length or subfragment **fusion** products
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nucleotide sequence; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 155945-98-5, PN: US5962255 SEQID: 59 unclaimed DNA 156163-00-7 167728-69-0 167728-70-3 167728-71-4 167728-72-5 167728-73-6 167731-70-6 167731-74-0, PN: US5962255 SEQID: 56 unclaimed DNA 167731-75-1, PN: US5962255 SEQID: 57 unclaimed DNA 167731-76-2, PN: US5962255 SEQID: 58 unclaimed DNA 167731-77-3, PN: US5962255 SEQID: 60 unclaimed DNA 167731-78-4, PN: US5962255 SEQID: 61 unclaimed DNA

167731-79-5 167731-80-8 167731-81-9 167732-10-7 167732-11-8, PN: US5962255 SEQID: 551 unclaimed DNA 167732-12-9 167732-13-0 167732-14-1, PN: US5962255 SEQID: 554 unclaimed DNA 167732-15-2, PN: US5962255 SEQID: 555 unclaimed DNA 167732-16-3 167732-17-4 167732-18-5 167732-19-6, PN: US5962255 SEQID: 98 unclaimed DNA 167732-20-9, PN: US5962255 SEQID: 572 unclaimed DNA 167732-21-0 167732-22-1, PN: US5962255 SEQID: 574 unclaimed DNA 195164-37-5 217893-77-1, GenBank A63614 217893-78-2, GenBank A63615 217893-79-3, GenBank A63616 217893-80-6, GenBank A63617 217893-81-7, GenBank A63618 217893-82-8, GenBank A63619 217893-83-9, GenBank A63620 217893-84-0, GenBank A63621 217893-85-1, GenBank A63622 217893-86-2, GenBank A63624 217893-89-5, GenBank A63627 217893-90-8, GenBank A63628 217893-91-9, GenBank A63629 217893-92-0, GenBank A63630 367319-52-6 367319-53-7 367319-54-8 367319-55-9 367319-56-0 367319-57-1 367319-58-2 367319-59-3 367319-60-6 367319-61-7 367319-62-8 367319-63-9 367319-64-0 367319-65-1 367319-66-2
RL: PRP (Properties)
(unclaimed nucleotide sequence; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 122024-47-9 131748-18-0 229477-44-5 244008-03-5, PN: WO9947540 SEQID: 3 unclaimed DNA 244008-06-8, PN: WO9947540 SEQID: 4 unclaimed DNA 244008-07-9, PN: WO9947540 SEQID: 5 unclaimed DNA 244008-08-0, PN: WO9947540 SEQID: 6 unclaimed DNA 244008-09-1, PN: WO9947540 SEQID: 7 unclaimed DNA 244008-12-6, 8: PN: WO0183510 SEQID: 8 unclaimed DNA 244008-13-7, PN: WO9947540 SEQID: 9 unclaimed DNA 244008-14-8, PN: WO9947540 SEQID: 10 unclaimed DNA 367273-46-9 367273-47-0 367273-48-1
RL: PRP (Properties)
(unclaimed sequence; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

L66 ANSWER 10 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:780938 HCAPLUS
DN 135:322686
ED Entered STN: 26 Oct 2001
TI **Albumin fusion** proteins with therapeutic proteins for improved **shelf-life**
IN **Rosen, Craig A.**; Sadeghi, Homayoun; Prior, Christopher P.; Turner, Andrew John
PA **Human Genome Sciences, Inc., USA**; Principia Pharmaceutical Corporation
SO PCT Int. Appl., 328 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K001-00
ICS A01N037-18
CC 63-3 (Pharmaceuticals)
Section cross-reference(s): 3, 15
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001079258	A1	20011025	WO 2001-US12008	20010412

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

	EP 1274720	A1	20030115	EP 2001-932549	20010412
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2003125247	A1	20030703	US 2001-833041	20010412
	US 2003171267	A1	20030911	US 2001-833117	20010412
	JP 2003530838	T2	20031021	JP 2001-576855	20010412
	US 2003199043	A1	20031023	US 2001-832501	20010412
	US 2003219875	A1	20031127	US 2001-833118	20010412
	US 2004010134	A1	20040115	US 2001-833245	20010412
PRAI	US 2000-229358P	P	20000412		
	US 2000-199384P	P	20000425		
	US 2000-256931P	P	20001221		
	WO 2001-US12008	W	20010412		

AB The present invention encompasses **fusion** proteins of **albumin** with various therapeutic proteins, and in particular, with interleukin 2, calcitonin, growth hormone-releasing factor, **interferon** β , parathyroid hormine, and insulin-like growth factor 1. Therapeutic proteins may be stabilized to extend the **shelf-life**, and/or to retain the therapeutic protein's activity for extended periods of time in solution, in vitro and/or in vivo, by genetically or chemical **fusing** or conjugating the therapeutic protein to **albumin** or a fragment or variant of **albumin** . Use of **albumin fusion** proteins may also reduce the need to formulate the protein solns. with large excesses of carrier proteins to prevent loss of therapeutic proteins due to factors such as binding to the container. Nucleic acid mols. encoding the **albumin fusion** proteins of the invention are also encompassed by the invention, as are vectors containing these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the **albumin fusion** proteins of the invention and using these nucleic acids, vectors, and/or host cells. Thus, plasmid vectors are constructed in which DNA encoding the desired therapeutic protein may be inserted for expression of the **albumin fusion** proteins in yeast (pPPC0005) and mammalian cells (pC4:HSA). Yeast-derived signal sequences from Saccharomyces cerevisiae invertase SUC2 gene, or the stanniocalcin or native human serum **albumin** signal peptides, are used for secretion in yeast or mammalian systems, resp. Thus, the **fusion** product of human growth hormone with residues 1-387 of human serum **albumin** retains essentially intact biol. activity after 5 wk of incubation in tissue culture media at 37°, whereas **recombinant** human growth hormone used as control lost its biol. activity in the first week. Although the potency of the **albumin fusion** proteins is slightly lower than the unfused counterparts in rapid bioassays, their biol. stability results in much higher biol. activity in the longer term in vitro assay or in vivo assays. Addnl., the present invention encompasses pharmaceutical compns. comprising **albumin fusion** proteins and methods of treating, preventing, or ameliorating diseases, disorders or conditions using **albumin fusion** proteins of the invention.

ST **albumin fusion** therapeutic protein **shelflife**

IT Hepatitis
(C, agents for treatment of; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Antitumor agents
(Kaposi's sarcoma; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Antitumor agents
(acute myelogenous leukemia; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Anti-AIDS agents
Antidiabetic agents

Antirheumatic agents
Drug delivery systems
Gene therapy
Immunosuppressants
Molecular cloning
(**albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Cell adhesion molecules
Cytokines
Enzymes, biological studies
Fusion proteins (chimeric proteins)
Growth factors, animal
Interferons
Interleukin 2
Synthetic gene
Tumor necrosis factor receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Signal peptides
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(for improved secretion in yeast or mammalian cells; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Intestine, disease
(**inflammatory**, agents for treatment of; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Kidney, neoplasm
Lung, neoplasm
Ovary, neoplasm
(inhibitors; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Antitumor agents
(kidney; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Antitumor agents
(leukemia; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Antitumor agents
(lung; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Animal cell
(mammalian, **recombinant** expression host; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Antitumor agents
(melanoma, metastasis; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Antitumor agents
(melanoma; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Antitumor agents
(non-Hodgkin's lymphoma; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Antitumor agents
(ovary; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT Plasmid vectors
(pC4:HSA, for mammalian cell expression; **albumin fusion** proteins with therapeutic proteins for improved

shelf-life)
IT Plasmid vectors
(pPPC0005, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
IT Plasmid vectors
(pScCHSa, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
IT Plasmid vectors
(pScNHSA, for yeast expression; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
IT Saccharomyces cerevisiae
Yeast
(**recombinant** expression host; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
IT Kidney, neoplasm
(renal-cell carcinoma, metastasis, inhibitors; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
IT Antitumor agents
(renal-cell carcinoma, metastasis; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
IT **Albumins, biological studies**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(serum; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(signal sequence, for improved secretion in yeast or mammalian cells; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
IT Antibodies
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(single chain; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
IT Multiple sclerosis
(therapeutic agents; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(therapeutic; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
IT **Interferons**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(α ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
IT **Interferons**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(β ; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)
IT 9002-64-6P, Parathyroid hormone 9002-67-9P, Luteinizing hormone 9002-68-0P, FSH 9002-72-6P, Growth hormone 9004-10-8P, Insulin, biological studies 9007-12-9P, Calcitonin 9034-39-3P, Growth

hormone-releasing factor 11096-26-7P, Erythropoietin 67763-96-6P, Insulin-like growth factor 1 83869-56-1P, GM-CSF 143011-72-7P, G-CSF
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 127361-02-8DP, **Albumin** (human blood serum clone HSA-II/HSA-I-A protein moiety reduced), full-length or subfragment **fusion** products
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nucleotide sequence; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 156163-00-7 217893-77-1, GenBank A63614 217893-78-2, GenBank A63615 217893-79-3, GenBank A63616 217893-80-6, GenBank A63617 217893-81-7, GenBank A63618 217893-82-8, GenBank A63619 217893-83-9, GenBank A63620 217893-84-0, GenBank A63621 217893-85-1, GenBank A63622 217893-86-2, GenBank A63624 217893-89-5, GenBank A63627 217893-90-8, GenBank A63628 217893-91-9, GenBank A63629 217893-92-0, GenBank A63630 244008-03-5, PN: WO9947540 SEQID: 3 unclaimed DNA 244008-06-8, PN: WO9947540 SEQID: 4 unclaimed DNA 244008-07-9, PN: WO9947540 SEQID: 5 unclaimed DNA 244008-08-0, PN: WO9947540 SEQID: 6 unclaimed DNA 244008-09-1, PN: WO9947540 SEQID: 7 unclaimed DNA 244008-12-6, 8: PN: WO0183510 SEQID: 8 unclaimed DNA 244008-13-7, PN: WO9947540 SEQID: 9 unclaimed DNA 244008-14-8, PN: WO9947540 SEQID: 10 unclaimed DNA 367319-52-6 367319-53-7 367319-54-8 367319-55-9 367319-56-0 367319-57-1 367319-58-2 367319-59-3 367319-60-6 367319-61-7 367319-62-8 367319-63-9 367319-64-0 367319-65-1 367319-66-2 367319-67-3
RL: PRP (Properties)
(unclaimed nucleotide sequence; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 367510-76-7
RL: PRP (Properties)
(unclaimed protein sequence; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

IT 131748-18-0 367273-46-9 367273-47-0 367273-48-1
RL: PRP (Properties)
(unclaimed sequence; **albumin fusion** proteins with therapeutic proteins for improved **shelf-life**)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Beth Israel Hospital Association; WO 9618412 A1 1996 HCAPLUS
(2) Lee; Pharm Dev Tech 1999, V4(2), P269 HCAPLUS
(3) Rhone-Poulenc Rorer S A; WO 9315199 A1 1993 HCAPLUS
(4) Rhone-Poulenc Rorer S A; WO 9315211 A1 1993 HCAPLUS
(5) Takahashi; Peptides 1997, V18(3), P439 HCAPLUS
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L66 ANSWER 11 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:763025 HCAPLUS
DN 135:335111
ED Entered STN: 19 Oct 2001
TI Albumin fusion proteins with therapeutic proteins for improved shelf-life
IN Rosen, Craig A.; Haseltine, William A.
PA Human Genome Sciences, Inc., USA
SO PCT Int. Appl., 2102 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07H021-04
CC 63-3 (Pharmaceuticals)

Section cross-reference(s): 3, 15

FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001077137	A1	20011018	WO 2001-US11988	20010412
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1276756	A1	20030122	EP 2001-944114	20010412
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2003125247	A1	20030703	US 2001-833041	20010412
	US 2003171267	A1	20030911	US 2001-833117	20010412
	US 2003199043	A1	20031023	US 2001-832501	20010412
	US 2003219875	A1	20031127	US 2001-833118	20010412
	US 2004010134	A1	20040115	US 2001-833245	20010412
PRAI	US 2000-229358P	P	20000412		
	US 2000-199384P	P	20000425		
	US 2000-256931P	P	20001221		
	WO 2001-US11988	W	20010412		

AB The present invention encompasses fusion proteins of albumin with various therapeutic proteins. Therapeutic proteins may be stabilized to extend the shelf-life, and/or to retain the therapeutic protein's activity for extended periods of time in solution, in vitro and/or in vivo, by genetically or chemical fusing or conjugating the therapeutic protein to albumin or a fragment or variant of albumin. Use of albumin fusion proteins may also reduce the need to formulate the protein solns. with large excesses of carrier proteins to prevent loss of therapeutic proteins due to factors such as binding to the container. Nucleic acid mols. encoding the albumin fusion proteins of the invention are also encompassed by the invention, as are vectors containing these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the albumin fusion proteins of the invention and using these nucleic acids, vectors, and/or host cells. Thus, plasmid vectors are constructed in which DNA encoding the desired therapeutic protein may be inserted for expression of the albumin fusion proteins in yeast (pPPC0005) and mammalian cells (pC4:HSA). Yeast-derived signal sequences from Saccharomyces cerevisiae invertase SUC2 gene, or the stanniocalcin or native human serum albumin signal peptides, are used for secretion in yeast or mammalian systems, resp. Thus, the fusion product of human growth hormone with residues 1-387 of human serum albumin retains essentially intact biol. activity after 5 wk of incubation in tissue culture media at 37°, whereas recombinant human growth hormone used as control lost its biol. activity in the first week. Although the potency of the albumin fusion proteins is slightly lower than the unfused counterparts in rapid bioassays, their biol. stability results in much higher biol. activity in the longer term in vitro assay or in vivo assays. Addnl., the present invention encompasses pharmaceutical compns. comprising albumin fusion proteins and methods of treating, preventing, or ameliorating diseases, disorders or conditions using albumin fusion proteins of the invention.

ST albumin fusion therapeutic protein shelflife

IT Drug delivery systems
Gene therapy
Molecular cloning
(albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT Cell adhesion molecules

Cytokines
Enzymes, biological studies
Fusion proteins (chimeric proteins)
Growth factors, animal
Interferons
Synthetic gene
Tumor necrosis factor receptors
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT Signal peptides
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(for improved secretion in yeast or mammalian cells; albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT Animal cell
(mammalian, recombinant expression host; albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT Plasmid vectors
(pC4:HSA, for mammalian cell expression; albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT Plasmid vectors
(pPPC0005, for yeast expression; albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT Plasmid vectors
(pScCHSa, for yeast expression; albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT Plasmid vectors
(pScNHSA, for yeast expression; albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT Saccharomyces cerevisiae
Yeast
(recombinant expression host; albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT Albumins, biological studies
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(serum; albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT Genetic element
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(signal sequence, for improved secretion in yeast or mammalian cells; albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT Antibodies
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(single chain; albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT Proteins, specific or class
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(therapeutic; albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT Interferons
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(α; albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT 9002-67-9P, Luteinizing hormone 9002-68-0P, FSH 9002-72-6P, Growth hormone 9004-10-8P, Insulin, biological studies 11096-26-7P,

Erythropoietin 67763-96-6P, Insulin-like growth factor 1 83869-56-1P, GM-CSF 143011-72-7P, G-CSF
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT 127361-02-8DP, Albumin (human blood serum clone HSA-II/HSA-I-A protein moiety reduced), full-length or subfragment fusion products
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nucleotide sequence; albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT 155945-98-5, PN: US5962255 SEQID: 59 unclaimed DNA 156163-00-7 167728-69-0 167728-70-3 167728-71-4 167728-72-5 167728-73-6 167731-70-6 167731-74-0, PN: US5962255 SEQID: 56 unclaimed DNA 167731-75-1, PN: US5962255 SEQID: 57 unclaimed DNA 167731-76-2, PN: US5962255 SEQID: 58 unclaimed DNA 167731-77-3, PN: US5962255 SEQID: 60 unclaimed DNA 167731-78-4, PN: US5962255 SEQID: 61 unclaimed DNA 167731-79-5 167731-80-8 167731-81-9 167732-10-7 167732-11-8, PN: US5962255 SEQID: 551 unclaimed DNA 167732-12-9 167732-13-0 167732-14-1, PN: US5962255 SEQID: 554 unclaimed DNA 167732-15-2, PN: US5962255 SEQID: 555 unclaimed DNA 167732-16-3 167732-17-4 167732-18-5 167732-19-6, PN: US5962255 SEQID: 98 unclaimed DNA 167732-20-9, PN: US5962255 SEQID: 572 unclaimed DNA 167732-21-0 167732-22-1, PN: US5962255 SEQID: 574 unclaimed DNA 195164-37-5 217893-77-1, GenBank A63614 217893-78-2, GenBank A63615 217893-79-3, GenBank A63616 217893-80-6, GenBank A63617 217893-81-7, GenBank A63618 217893-82-8, GenBank A63619 217893-83-9, GenBank A63620 217893-84-0, GenBank A63621 217893-86-2, GenBank A63624 217893-89-5, GenBank A63627 217893-90-8, GenBank A63628 217893-91-9, GenBank A63629 217893-92-0, GenBank A63630 367319-52-6 367319-53-7 367319-54-8 367319-55-9 367319-56-0 367319-57-1 367319-58-2 367319-59-3 367319-60-6 367319-61-7 367319-62-8 367319-64-0 367319-65-1 367319-66-2 367985-08-8
RL: PRP (Properties)
(unclaimed nucleotide sequence; albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT 135688-15-2, Complement C1q (human clone pC1qA8.0E A-chain precursor protein moiety reduced) 151187-86-9 160405-14-1 160405-30-1 161477-27-6 180191-50-8 208473-02-3 208668-41-1 208885-10-3, Gremlin (human) 209402-85-7 211509-29-4, Protein (human clone KIAA0626 reduced) 212701-83-2, Antigen JTT.1 (human) 213471-70-6, Protein zsig32 (human) 213537-31-6 221369-74-0 222536-56-3 222614-92-8 222963-77-1, Protein (human brain gene KIAA0879) 225371-37-9 227183-97-3 228856-39-1 228859-29-8, Protein (human gene PG1) 229483-48-1 229483-74-3 229965-62-2 234086-26-1 235768-74-8 236732-55-1 243122-23-8 243122-49-8 244028-96-4 244295-44-1 249910-22-3 250154-03-1 251929-91-6 252050-85-4 252051-18-6 252051-68-6 252366-50-0 252366-55-5 253418-72-3 253418-75-6 253418-83-6 253419-18-0 253419-34-0 253419-41-9 253603-07-5 256325-28-7 257854-54-9 259163-54-7 259163-79-6 260382-31-8 270051-56-4, Hydrolase (human Incyte clone 1297034) 270051-58-6, Hydrolase (human Incyte clone 1702211) 270054-17-6, Platelet-derived growth factor D (human) 271753-29-8 277336-39-7 277762-05-7 278626-74-7, Osteoglycin (human gene OGN) 287216-11-9 291585-61-0 291797-63-2 292066-57-0 292656-62-3 292658-62-9 292883-48-8 293308-26-6 294683-12-8 294900-23-5 294906-53-9 297774-95-9 300429-08-7 300431-40-7 300619-65-2 300620-75-1 301252-55-1 301257-58-9 303071-71-8 309763-61-9 312976-96-8 314326-43-7 318300-05-9, Protein (human clone PSEC0021) 318301-14-3, Protein (human clone PSEC0133) 318301-24-5, Protein (human clone PSEC0143) 318301-57-4, Protein (human clone PSEC0170) 321452-27-1 321452-28-2 321452-29-3 321452-30-6 321452-31-7 321452-32-8 321452-33-9

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RL: PRP (Properties)
(unclaimed protein sequence; albumin fusion proteins with therapeutic proteins for improved shelf-life)

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RL: PRP (Properties)
(unclaimed protein sequence; albumin fusion proteins with therapeutic proteins for improved shelf-life)

IT 339216-28-3 339216-29-4 339216-30-7 339216-31-8 339216-32-9
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RL: PRP (Properties)
(unclaimed protein sequence; albumin fusion proteins with therapeutic proteins for improved shelf-life)

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RL: PRP (Properties)
(unclaimed protein sequence; albumin fusion proteins with therapeutic proteins for improved shelf-life)

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RL: PRP (Properties)
(unclaimed protein sequence; albumin fusion proteins with therapeutic proteins for improved shelf-life)

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RL: PRP (Properties)
(unclaimed protein sequence; albumin fusion proteins with therapeutic proteins for improved shelf-life)

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(unclaimed protein sequence; albumin fusion proteins with therapeutic proteins for improved shelf-life)

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339526-48-6 339526-49-7 339527-59-2 339529-52-1 339529-55-4
339529-56-5 339529-57-6 339529-58-7 339529-59-8 339529-60-1
339529-61-2 339529-62-3 339529-64-5 339529-65-6 339540-74-8
339540-75-9 339540-76-0 339540-77-1 339540-78-2 339540-79-3
339540-80-6 339540-81-7 339540-82-8 339540-83-9 339541-20-7
339541-21-8 339541-23-0 339541-24-1 339541-25-2 339541-26-3
339541-27-4 339541-28-5 339565-68-3 339605-85-5 339613-93-3
340003-40-9 340003-41-0 340003-42-1 340003-43-2 340003-44-3
340003-45-4 340003-46-5 340003-47-6 340003-48-7 340255-72-3
340255-74-5 340255-75-6 340255-76-7 340255-77-8 340255-78-9
340255-79-0 340255-80-3 340255-81-4 340255-82-5 340255-83-6
340255-84-7 340256-43-1 340685-59-8 340773-66-2 340963-10-2
340963-11-3 352273-69-9 352273-70-2 353264-67-2 353264-68-3
367273-46-9 367273-47-0 367273-48-1 368941-64-4 368941-69-9
368941-87-1 368942-06-7 368942-11-4 368942-17-0 368942-20-5
368942-21-6 368942-30-7 368942-37-4 368942-41-0 368942-46-5
368942-51-2 368942-62-5 368942-72-7 368942-78-3 368942-81-8
368942-84-1 368943-09-3 368943-19-5 368943-25-3 368943-27-5
368943-30-0 368943-31-1 368943-58-2 368943-61-7 369386-27-6
369386-99-2 369387-03-1 369413-79-6 369414-52-8 369589-20-8
369593-28-2 369593-29-3 369593-30-6 369593-33-9 369593-41-9
369593-44-2 369593-45-3 369593-46-4 369638-87-9 369660-66-2
RL: PRP (Properties)
(unclaimed sequence; albumin fusion proteins with therapeutic proteins for improved shelf-life)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Delta Biotechnology Limited; EP 0322094 A1 1989 HCAPLUS
(2) Delta Biotechnology Limited; WO 9724445 A1 1997 HCAPLUS
(3) Human Genome Sciences Inc; WO 9734997 A1 1997 HCAPLUS

L66 ANSWER 12 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **2000:609058** HCAPLUS
DN **133:168425**
ED Entered STN: 01 Sep 2000
TI Suppository of **recombinant** human **interferon** .
alpha.2a
IN Chen, Weijia; Zheng, Hui; Zhang, Yan; Wang, Dongqian
PA Changchun Biological Product Inst., Ministry of Public Health, Peop. Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 5 pp.
CODEN: CNXXEV
DT Patent
LA Chinese
IC ICM A61K009-02
ICS A61K038-21
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CN 1230400	A	19991006	CN 1999-105589	19990415 <--
PRAI	CN 1999-105589		19990415 <--		

AB Suppository of **interferon** α 2a comprise **recombinant** human **interferon** α 2a solution (0.5 MIU per suppository) 14, glycerol 58, gelatin 26, and human serum **albumin** 2%. The preparation process involves mixing glycerol with gelatin, standing overnight, sterilizing for 20-30 min, cooling to 40-56Φ', adding **recombinant** human **interferon** . **alpha**.2a, and shaping.
ST **recombinant** human **interferon alpha** 2a suppository
IT **Albumins, biological studies**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(serum; suppository of **recombinant** human **interferon** α 2a)
IT Drug delivery systems
(suppositories; suppository of **recombinant** human **interferon** α 2a)
IT Anti-**inflammatory** agents
Antitumor agents
Antiviral agents
Skin, disease
(suppository of **recombinant** human **interferon** α 2a)
IT Gelatins, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(suppository of **recombinant** human **interferon** α 2a)
IT **Interferons**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α **-2a**, **recombinant** human; suppository of **recombinant** human **interferon** α **2a**)
IT 56-81-5, Glycerol, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(suppository of **recombinant** human **interferon** α 2a)

L66 ANSWER 13 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1999:783954** HCAPLUS
DN **132:26853**
ED Entered STN: 10 Dec 1999
TI **Recombinant** human **interferon** β -1A (**IFN-beta**-1A) formulation
IN Alam, John; Rogge, Mark; Goelz, Susan
PA Biogen, Inc., USA
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-21
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 15
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9962542	A1	19991209	WO 1998-US7242	19980529 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2333063	AA	19991209	CA 1998-2333063	19980529 <--
AU 9888225	A1	19991220	AU 1998-88225	19980529 <--
BR 9815966	A	20010228	BR 1998-15966	19980529 <--
EP 1082132	A1	20010314	EP 1998-939859	19980529 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002516874	T2	20020611	JP 2000-551797	19980529 <--
EE 200000694	A	20020617	EE 2000-200000694	19980529 <--
NO 2000006022	A	20010126	NO 2000-6022	20001128 <--
PRAI WO 1998-US7242	A	19980529 <--		

AB Liquid compns. comprising a buffer of pH about 7.2, **recombinant interferon-β** and 15 mg/mL of human serum **albumin**, and kits for parenteral administration comprising said compns. are disclosed.
ST **recombinant interferon beta** formulation
IT Medical goods
(alc. swabs; **recombinant** human **interferon** β -1A (**IFN-beta**-1A) formulation)
IT Medical goods
(bandages, adhesive; **recombinant** human **interferon** β -1A (**IFN-beta**-1A) formulation)
IT Buffers
Molecular cloning
Needles (tools)
Syringes
pH
(**recombinant** human **interferon** β -1A (**IFN-beta**-1A) formulation)
IT **Albumins, biological studies**
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(serum, human; **recombinant** human **interferon** β -1A (**IFN-beta**-1A) formulation)
IT **Interferons**
RL: BPN (Biosynthetic preparation); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); PROC (Process); USES (Uses)
(β ; **recombinant** human **interferon** β -1A (**IFN-beta**-1A) formulation)
IT 145258-61-3, **Interferon** β 1 (human fibroblast protein moiety)
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**recombinant** human **interferon** β -1A (**IFN-beta**-1A) formulation)
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Alam, J; Pharmaceutical Research 1997, V14(4), P546 HCAPLUS
(2) Anon; http://www.healthdirect.com/usenew/pressrel/p_biogel.htm 1996
(3) Salmon, P; Journal of Interferon and Cytokine Research 1996, V16(10), P759 HCAPLUS
(4) US Food and Drug Administration-Interferon Beta-1A, Biogen, Inc; http://www.fda.gov/cber/products/ifnbbio051796.htm, http://www.fda.gov/cber/label/infbbio051796lb.pdf 1998

L66 ANSWER 14 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1999:563880** HCAPLUS
DN **131:161626**
ED Entered STN: 08 Sep 1999
TI Oral **recombinant** human α **-interferon** compositions
IN Dong, Yilan; Cheng, Xiaogeng; Lin, Yuxin; Wang, Shiwen; Liu, Zhenhao; Duan, Li
PA Changchun Institute of Biological Products, Ministry of Public Health, Peop. Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 8 pp.
CODEN: CNXXEV
DT Patent
LA Chinese
IC ICM A61K038-21
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 15
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI CN 1116951	A	19960221	CN 1995-101216	19950125 <--
PRAI CN 1995-101216		19950125 <--		

AB Title compns. as antiviral agents contain **recombinant** human **alpha.-interferon** 100-500 IU, thymosin F5 isolated from calf's thymus gland 1-20 μg, stabilizers and conventional medical additives. The stabilizers are selected from human serum **albumin** , cattle serum **albumin**, β-cyclodextrin and PEG 800.
ST **recombinant** human **interferon** tablet antiviral
IT Antiviral agents
Stabilizing agents
(oral **recombinant** human α **-interferon** compns.)
IT Polyoxyalkylenes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral **recombinant** human α **-interferon** compns.)
IT Drug delivery systems
(oral; oral **recombinant** human α **-interferon** compns.)
IT **Albumins, biological studies**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(serum, human or bovine; oral **recombinant** human α **-interferon** compns.)
IT Drug delivery systems

(tablets; oral **recombinant** human α - **interferon** compns.)

IT **Interferons**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α , **recombinant** human; oral **recombinant** human α -**interferon** compns.)

IT **Interferons**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α -**2a**, **recombinant** human; oral **recombinant** human α -**interferon** compns.)

IT **Interferons**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α -**2b**, **recombinant** human; oral **recombinant** human α -**interferon** compns.)

IT **Interferons**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α **1**, **recombinant** human; oral **recombinant** human α -**interferon** compns.)

IT 61512-21-8, Thymosin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(F5; oral **recombinant** human α - **interferon** compns.)

IT 7585-39-9, β-Cyclodextrin 25322-68-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral **recombinant** human α -**interferon** compns.)

L66 ANSWER 15 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1997:756962** HCAPLUS
DN **128:16442**
ED Entered STN: 04 Dec 1997
TI Stabilization of **interferons** in aqueous solution for manufacture of sublingually administered tablets
IN Rothschild, Peter R.
PA Feronpatent Limited, Ire.; Rothschild, Peter R.
SO PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-21
ICS A61K009-20
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9741885	A1	19971113	WO 1997-IB531	19970509	<--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	AU 9724011	A1	19971126	AU 1997-24011	19970509	<--
	EP 920329	A1	19990609	EP 1997-919596	19970509	<--
	EP 920329	B1	20020925			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					

AT 224725 E 20021015 AT 1997-919596 19970509 <--
ES 2184084 T3 20030401 ES 1997-919596 19970509 <--
PRAI WO 1996-IB433 A 19960509 <--
WO 1997-IB531 W 19970509 <--

AB Natural and **recombinant interferons** are stabilized with bidistd. water, lactose, **albumin**, sodium mono- and dihydrogen phosphates, (C5H10O5)n, such as arabic gum, dissolved and diluted in 20 % ethanol solution to the fourth decimal by homeopathic method. The final solution is sprayed on to an excipient comprising of 20 % arabic gum, 30 % lactose and 50 % starch for manufacturing tablets of 100 mg each containing 200 I.U. of human alfa-**interferon**. The tablets are sublingually administered to the patient for treatment of viral **infections** sensitive to **interferon**. Preparation of sublingual tablets according above method is disclosed.

ST stabilization **interferon** polysaccharide sublingual pharmaceutical tablet

IT Hepatitis
(B; stabilization of **interferons** in aqueous solution for manufacture of sublingually administered tablets)

IT Hepatitis
(C; stabilization of **interferons** in aqueous solution for manufacture of sublingually administered tablets)

IT Therapy
(homeopathy; stabilization of **interferons** in aqueous solution for manufacture of sublingually administered tablets)

IT Antitumor agents
Stabilizing agents
(stabilization of **interferons** in aqueous solution for manufacture of sublingually administered tablets)

IT **Albumins, biological studies**
Interferons
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stabilization of **interferons** in aqueous solution for manufacture of sublingually administered tablets)

IT Drug delivery systems
(tablets, sublingual; stabilization of **interferons** in aqueous solution for manufacture of sublingually administered tablets)

IT **Infection**
(viral; stabilization of **interferons** in aqueous solution for manufacture of sublingually administered tablets)

IT **Interferons**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α ; stabilization of **interferons** in aqueous solution for manufacture of sublingually administered tablets)

IT **Interferons**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β ; stabilization of **interferons** in aqueous solution for manufacture of sublingually administered tablets)

IT **Interferons**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(γ; stabilization of **interferons** in aqueous solution for manufacture of sublingually administered tablets)

IT 63-42-3, Lactose 7558-79-4, Sodium monohydrogen phosphate 7558-80-7, Sodium dihydrogen phosphate 9000-01-5, Arabic gum 9005-25-8, Starch, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stabilization of **interferons** in aqueous solution for manufacture of sublingually administered tablets)

L66 ANSWER 16 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1996:635884** HCAPLUS
DN **125:308823**

ED Entered STN: 28 Oct 1996
TI Shelf-life of **recombinant** human **interferon** **alpha**.2b under different storage conditions
AU Barberia, Daisy; Vega, Maribel; Ferrero, Joel; Duany, Lady; Moya, Galina; Curras, Tania; Martinez, Maida; Cruz, Asterio; Gil, Miriela; Quintana, Marisel
CS Centro de Ingenieria Genetica y Biotecnologia, Havana, Cuba
SO Biotecnologia Aplicada (**1996**), 13(3), 190-194
CODEN: BTAPEP; ISSN: 0864-4551
PB Sociedad Iberolatinoamericana de Biotecnologia Aplicada a la Salud
DT Journal
LA Spanish
CC 63-5 (Pharmaceuticals)
AB The stability test studies under accelerated and normal storage conditions carried out with **recombinant** human alpha 2b **interferon** (hu-r alpha 2b IFN) in phosphate buffer 0.1M, pH 7.0, with and without **albumin**, in order to establish its shelf-life at refrigerating and frozen conditions. According to the accelerated study the authors concluded that no alterations will interfere with the recognition of hu-r alpha 2b IFN in ELISA in at least five years when stored at -70 or -20°. Otherwise, when stored at 4°, a loss of 10% may occur in one year. The authors corroborated this when the presence of new structures which might affect the protein immunol. recognition were detected by RP-HPLC. No stabilizing properties of **albumin** on hu-r alpha 2b IFN were observed at least when it is in phosphate buffer 0.1M, pH 7.0 and under accelerated storing conditions.
ST **interferon** stability denaturation freezing
IT **Albumins, biological studies**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(shelf-life of **recombinant** human **interferon** α 2b under different storage conditions)
IT **Interferons**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α **-2b**, shelf-life of **recombinant** human **interferon** α **2b** under different storage conditions)

L66 ANSWER 17 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1996:43019** HCAPLUS
DN **124:66661**
ED Entered STN: 23 Jan 1996
TI Stabilized β **-interferon** liquid formulations
IN Samaritani, Fabrizio; Natale, Patrizia
PA Applied Research Systems ARS Holding N.V., Neth.
SO PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-21
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9531213	A1	19951123	WO 1995-EP1825	19950515 <--
	W: AU, CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2190465	AA	19951123	CA 1995-2190465	19950515 <--
	AU 9526704	A1	19951205	AU 1995-26704	19950515 <--
	AU 704827	B2	19990506		
	EP 759775	A1	19970305	EP 1995-921749	19950515 <--
	EP 759775	B1	20000726		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 10500125	T2	19980106	JP 1995-529360	19950515 <--

	AT 194917	E	20000815	AT 1995-921749	19950515 <--
	ES 2148526	T3	20001016	ES 1995-921749	19950515 <--
PRAI	IT 1994-RM300	A	19940516 <--		
	WO 1995-EP1825	W	19950515 <--		

AB β -**Interferon** liquid formulations are stabilized with a polyol, a nonreducing sugar, or an amino acid. In particular, the formulations are stabilized with a polyol, such as mannitol. The formulations, preferably, furthermore comprise a buffer, such as acetate buffer at a pH 3-4 and human **albumin** at a min. quantity. The . **beta.-interferon** is preferably **recombinant.**

ST **interferon** soln stabilizer polyol **albumin** buffer; mannitol **albumin** acetate buffer **interferon** stability

IT Buffer substances and systems
(acetate; stabilized β -**interferon** liquid formulations)

IT **Albumins, biological studies**
Amino acids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stabilized β -**interferon** liquid formulations)

IT Carbohydrates and Sugars, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nonreducing, stabilized β -**interferon** liquid formulations)

IT Alcohols, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyhydric, stabilized β -**interferon** liquid formulations)

IT Pharmaceutical dosage forms
(solns., stabilized β -**interferon** liquid formulations)

IT **Interferons**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β , **recombinant;** stabilized β -**interferon** liquid formulations)

IT 56-40-6, Glycine, biological studies 57-50-1, Saccharose, biological studies 69-65-8, D-Mannitol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stabilized β -**interferon** liquid formulations)

L66 ANSWER 18 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1995:498838** HCAPLUS
DN **122:248213**
ED Entered STN: 20 Apr 1995
TI **Influence** of human serum **albumin** content in formulations on the bioequivalency of **interferon** alfa-2a given by subcutaneous injection in healthy male volunteers
AU Zhi, Jianguo; Teller, Stuart B.; Satoh, Hiroko; Koss-Twardy, Susan G.; Luke, David R.
CS Department of Clinical Pharmacokinetics, Hoffmann-La Roche, Inc., Nutley, NJ, 07110-1199, USA
SO Journal of Clinical Pharmacology (**1995**), 35(3), 281-4
CODEN: JCPCBR; ISSN: 0091-2700
DT Journal
LA English
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
AB To determine the **influence** of human serum **albumin** (HSA) content in formulations on the bioequivalency of **recombinant interferon** α 2a, a double-blind, randomized, two-way crossover study was conducted in 24 healthy male volunteers. Subjects received a single s.c. injection of 18 million IU of Roferon-A reconstituted with either the diluent containing 10 mg of HSA or the HSA-free diluent; final HSA contents in the 2 formulations were 15 and 5 mg, resp.

Administration of the 2 formulations resulted in similar 48-h Roferon-A serum concentration-time profiles and comparable frequency and intensity of adverse events. The statistical anal. using the two one-sided tests procedure showed that both formulations were bioequivalent for pharmacokinetic parameters such as Cmax, tmax, AUC48, and AUC. Thus, a threefold change in HSA content in formulations does not alter the bioequivalency of Roferon-A.

ST **interferon** bioavailability bioequivalence injection **albumin**

IT Drug bioavailability
(human serum **albumin** effect on bioequivalence of **recombinant interferon** α 2a from s.c. injection in humans)

IT **Albumins, biological studies**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human serum **albumin** effect on bioequivalence of **recombinant interferon** α 2a from s.c. injection in humans)

IT Pharmaceutical dosage forms
(injections, s.c., human serum **albumin** effect on bioequivalence of **recombinant interferon** α 2a from s.c. injection in humans)

IT **Interferons**
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(α **-2a**, human serum **albumin** effect on bioequivalence of **recombinant interferon** α **2a** from s.c. injection in humans)

L66 ANSWER 19 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1994:6892** HCAPLUS
DN **120:6892**
ED Entered STN: 08 Jan 1994
TI Novel **recombinant** human **IFN-β** , its preparation, and pharmaceutical compositions containing it
IN Siklosi, Thomas; Joester, Karl-eduard; Hofer, Hans
PA BIOFERON Biochemische Substanzen GmbH und Co, Germany
SO Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DT Patent
LA German
IC ICM C07K015-26
ICS C07K003-28; A61K037-66
CC 16-2 (Fermentation and Bioindustrial Chemistry)
Section cross-reference(s): 15

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 529300	A1	19930303	EP 1992-112427	19920721 <--
	EP 529300	B1	19981014		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE				
	DE 4128319	A1	19930304	DE 1991-4128319	19910827 <--
	AT 172206	E	19981015	AT 1992-112427	19920721 <--
	ES 2121804	T3	19981216	ES 1992-112427	19920721 <--
PRAI	DE 1991-4128319		19910827 <--		

AB A **recombinant** human β **-interferon** (**IFN-β**) produced in mammalian cells, whose oligosaccharide component comprises biantennary ≥60%, triantennary ≥15%, and tetraantennary 0-5% and contains fucose and ≥80% sialic acid, is useful for treatment of tumors, especially Kaposi's sarcoma. Thus, **recombinant IFN-β** was produced in transfected CHO BIC 8622 cells in MEM containing fetal calf serum and secreted into the medium in a yield of 1 + 105-1 + 106 IU/L. The

IFN-β was purified by liquid-liquid extraction in a PEG 2000-salt solution system, affinity chromatog. on Blue Dextran FF, metal chelate chromatog. on a Zn2+-loaded chelating Sepharose column, and size exclusion chromatog. on Sephacryl. The product showed a purity of >99% and high stability at -20, +15, or +25° when mixed with buffered human serum **albumin** and stored for 1-4 wk. Enzymic removal of terminal sialic acid residues diminished the stability.

ST **recombinant beta interferon** purifn

IT Polyoxyalkylenes, biological studies
Salts, biological studies
RL: BIOL (Biological study)
(in β -**interferon** purification, by partition)

IT Oligosaccharides
Sialic acids
RL: BIOL (Biological study)
(of **recombinant** β -**interferon**)

IT Chromatography, gel
(of β -**interferon**)

IT Partition
(of β -**interferon**, in polyalkylene glycol/dextran and polyalkylene glycol/salt systems)

IT Neoplasm inhibitors
(**recombinant** β -**interferon**)

IT Dyes
(β -**interferon** affinity chromatog. on)

IT Animal cell line
(CHO, **recombinant** β -**interferon** manufacture with)

IT Neoplasm inhibitors
(Kaposi's sarcoma, **recombinant** β -**interferon** as)

IT Chromatography, column and liquid
(affinity, of β -**interferon**, on dye)

IT Coordination compounds
RL: BIOL (Biological study)
(chelates, stationary phases containing, for β -**interferon** chromatog.)

IT **Interferons**
RL: BIOL (Biological study)
(β , purification of **recombinant**, for Kaposi's sarcoma treatment)

IT 12236-82-7 148498-83-3, Blue Sepharose FF 57-55-6, 1,2-Propanediol, uses 107-21-1, 1,2-Ethanediol, uses
RL: BIOL (Biological study)
(in β -**interferon** purification, by affinity chromatog.)

IT 56-40-6, Glycine, uses 71-00-1, Histidine, uses 288-32-4, Imidazole, uses
RL: USES (Uses)
(in β -**interferon** purification, by metal chelate chromatog.)

IT 62-76-0, Sodium oxalate 68-04-2, Sodium citrate 25322-68-3, Polyethylene glycol 25322-69-4, Polypropylene glycol 7447-40-7, Potassium chloride (KCl), uses 7447-41-8, Lithium chloride, uses 7558-79-4, Disodium phosphate 7558-80-7, Sodium dihydrogen phosphate 7647-14-5, Sodium chloride, uses 7681-11-0, Potassium iodide, uses 7681-82-5, Sodium iodide, uses 7757-82-6, Sodium sulfate, uses 7758-11-4, Dipotassium phosphate 7778-80-5, Potassium sulfate, uses 7783-20-2, Ammonium sulfate, uses 9004-54-0, Dextran, uses 12125-02-9, Ammonium chloride, uses
RL: BIOL (Biological study)
(in β -**interferon** purification, by partition)

IT 131-48-6, N-Acetylneuraminic acid 1113-83-3 2438-80-4, Fucose

32181-59-2, N-Acetyllactosamine 78392-81-1 83412-55-9 84813-89-8
123618-73-5 131432-29-6 148553-76-8 148553-77-9 148553-78-0
148553-79-1 148553-80-4 148553-81-5 148614-65-7 148615-15-0
RL: BIOL (Biological study)
(of **recombinant β -interferon**)
IT 7440-02-0D, Nickel, chelates 7440-48-4D, Cobalt, chelates 7440-50-8D,
Copper, chelates 7440-66-6D, Zinc, chelates 12774-36-6, Sephadex G150
97599-42-3, Superose 12 119332-87-5, Sephacryl S 200 High Resolution
148499-25-6, TSK-SW 3000
RL: BIOL (Biological study)
(**β -interferon** purification by chromatog. on)

L66 ANSWER 20 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1992:468225** HCAPLUS
DN **117:68225**
ED Entered STN: 23 Aug 1992
TI Human **β -interferon** incubated with muscle homogenate is protected by **albumin** but not by proteinase inhibitors
AU Paulesu, L.; Pessina, G. P.; Bocci, V.
CS Inst. Gen. Physiol., Univ. Siena, Siena, 53100, Italy
SO Proceedings of the Society for Experimental Biology and Medicine (**1992**), 200(3), 414-17
CODEN: PSEBAA; ISSN: 0037-9727
DT Journal
LA English
CC 15-5 (Immunochemistry)
Section cross-reference(s): 1
AB The scarce bioavailability of **β -interferon** (**IFN-β**) after i.m. administration is probably due either to the binding of **IFN-β** to the interstitial matrix, or to lymphatic absorption and/or to local breakdown by lysosomal proteinases from muscle. In this work, the authors first showed that after i.m. injection, the apparent bioavailability of natural human **IFN-β** is about 10% of that of **recombinant IFN-α** 2 and then they evaluated the effects of proteinase inhibitors and **albumin** on **IFN-β** incubated at 37° with muscle homogenate. IFN biol. activity decreased spontaneously by about 20% after incubation for 6 h at 37° in Hanks' solution, but it was almost completely lost after incubation with muscle homogenate. Proteinase inhibitors (α1-antitrypsin, α2-macroglobulin, aprotinin, soybean trypsin inhibitor, leupeptin, EP-459, and EP-475) failed to block the inactivation of **IFN-β** by muscle proteinases, whereas **albumin** exerted a partial but consistent protection.
ST **interferon beta** bioavailability muscle **albumin** ; proteinase inhibitor **interferon beta** bioavailability
IT Muscle, metabolism
(**interferon-β** of humans inactivation by, **albumin** and proteinase inhibitors effect on)
IT **Albumins, biological studies**
RL: BIOL (Biological study)
(muscle inactivation of human **interferon-β** inhibition by)
IT **Interferons**
RL: BIOL (Biological study)
(**β** , muscle inactivation of human, **albumin** and proteinase inhibitors effect on)
IT 138674-34-7, Cysteine proteinase inhibitor 139691-92-2, Serine proteinase inhibitor
RL: BIOL (Biological study)
(muscle inactivation of human **interferon-β** response to)

L66 ANSWER 21 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1991:478932** HCAPLUS
DN **115:78932**
ED Entered STN: 23 Aug 1991
TI Stable formulations of lipophilic **recombinant** proteins
IN Fernandes, Peter M.; Taforo, Terrance
PA Cetus Corp., USA
SO U.S., 20 pp. Cont.-in-part of U.S. Ser. No. 752,403.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K037-02
ICS A61K045-02
NCL 424085200
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 16
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4992271	A	19910212	US 1985-775751	19850913 <--
	US 4462940	A	19840731	US 1983-495896	19830518 <--
	CA 1339707	A1	19980310	CA 1986-516417	19860820 <--
	AU 8662642	A1	19870319	AU 1986-62642	19860912 <--
	AU 590896	B2	19891123		
	EP 215658	A2	19870325	EP 1986-307070	19860912 <--
	EP 215658	A3	19890208		
	EP 215658	B1	19940601		
	R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
	AT 106247	E	19940615	AT 1986-307070	19860912 <--
	JP 62067032	A2	19870326	JP 1986-215063	19860913 <--
	JP 06004542	B4	19940119		
	US 5643566	A	19970701	US 1995-474769	19950607 <--
PRAI	US 1982-422421		19820923 <--		
	US 1983-495896		19830518 <--		
	US 1984-592077		19840323 <--		
	US 1985-752403		19850705 <--		
	US 1985-775751		19850913 <--		
	EP 1986-307070		19860912 <--		
	US 1986-923425		19861027 <--		
	US 1992-865411		19920507 <--		
	US 1994-266832		19940628 <--		

AB An improved process for recovering and purifying lipophilic **recombinant** proteins such as human β - **interferon** and interleukin-2 (IL-2) from their hosts yields a protein preparation which is formulated into a stable pharmaceutical composition having a therapeutically effective amount of the biol. active **recombinant** lipophilic protein dissolved in a nontoxic, inert, therapeutically compatible aqueous based carrier medium at a pH of 6.8 to 7.8. The medium also contains a stabilizer for the protein, such as human serum **albumin** and human plasma protein fraction. IL-2 produced by **recombinant** Escherichia coli was purified by a series of steps and formulated with human serum **albumin** (final concentration 2.5%) at pH 2.58.
ST interleukin Escherichia **albumin** stabilizer; **interferon** **recombinant** **albumin** formulation
IT Escherichia coli
(**beta-interferons** and interleukin 2 from)
IT Proteins, biological studies
RL: BIOL (Biological study)
(of blood plasma, as stabilizers for **recombinant** interleukin 2-containing pharmaceutical compns.)

IT Pharmaceutical dosage forms
(of **recombinant** β **-interferons** and
interleukin 2, stabilizers in, **albumins** and sugars as)
IT **Albumins, biological studies**
RL: BIOL (Biological study)
(stabilizers, for **recombinant** interleukin 2-containing
pharmaceutical compns.)
IT Lymphokines and Cytokines
RL: BIOL (Biological study)
(interleukin 2, **recombinant**, from Escherichia coli,
stabilized formulations of, **albumins** and sugars in)
IT **Interferons**
RL: BIOL (Biological study)
(β , **recombinant**, from Escherichia coli,
stabilized formulations of, **albumins** and sugars in)
IT 69-65-8, Mannitol
RL: BIOL (Biological study)
(stabilizer, for **recombinant** interleukin-2 containing
pharmaceutical composition)
IT 50-99-7, Dextrose, biological studies
RL: BIOL (Biological study)
(stabilizer, for **recombinant** β -
interferon-containing pharmaceutical composition)

L66 ANSWER 22 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1990:153049** HCAPLUS
DN **112:153049**
ED Entered STN: 28 Apr 1990
TI Use of human serum **albumin** signal peptide in **recombinant** protein manufacture and secretion with yeast
IN Hayasuke, Naofumi; Nakagawa, Yukimitsu; Ishida, Yutaka; Okabayashi, Ken; Murakami, Kohji; Tsutsui, Kiyoshi; Ikegaya, Kazuo; Minamino, Hitoshi; Ueda, Sadao; et al.
PA Green Cross Corp., Japan
SO Eur. Pat. Appl., 35 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM C12N015-00
ICS C12P021-00
CC 3-4 (Biochemical Genetics)
FAN.CNT 1

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE	
PI	EP 319641	A1	19890614		EP 1988-107087	19880503	<--
	EP 319641	B1	19930922				
	R: BE, CH, DE, ES, FR, GB, IT, LI, NL, SE						
	JP 02167095	A2	19900627		JP 1988-103339	19880426	<--
	JP 2791418	B2	19980827				
	CA 1326217	A1	19940118		CA 1988-565766	19880503	<--
	ES 2059428	T3	19941116		ES 1988-107087	19880503	<--
	KR 9705250	B1	19970414		KR 1988-5553	19880513	<--
	US 5503993	A	19960402		US 1995-445783	19950522	<--
PRAI	JP 1987-306674	A	19871202	<--			
	JP 1988-45605	A	19880226	<--			
	US 1988-190553	B1	19880505	<--			
	US 1992-913785	B1	19920630	<--			

OS MARPAT 112:153049
AB A method for producing and secreting proteins with yeast comprises transformation of the yeast with a **chimeric** gene for a human **albumin** signal peptide and the coding sequence for the desired protein and expression of the gene. Plasmid pNH008, containing the GAL1 promoter linked to a synthetic human serum **albumin** signal

sequence **fused** to the mature human serum **albumin** gene and the pho5 terminator, was constructed. Saccharomyces cerevisiae AH22 transformed with this plasmid produced 160 mg **albumin**/L culture medium after 48 h incubation.

ST protein secretion yeast **albumin** signal peptide; Saccharomyces human **albumin** manuf secretion

IT Saccharomyces cerevisiae
(human serum **albumin** manufacture and secretion with, **albumin** signal peptide in)

IT Molecular cloning
(in yeast, human serum **albumin** signal sequence in)

IT **Albumins, preparation**
RL: PREP (Preparation)
(manufacture of, of human, with yeast, human serum **albumin** signal peptide in)

IT Lymphokines and Cytokines
RL: PROC (Process)
(manufacture of, with yeast, human serum **albumin** signal peptide in)

IT Protein sequences
(of **albumin** signal peptide analogs, of human)

IT Yeast
(**recombinant** protein secretion from, signal peptide of human serum **albumin** in)

IT Deoxyribonucleic acid sequences
(**albumin**-specifying, signal peptide analog, of human)

IT Gene and Genetic element
RL: BIOL (Biological study)
(**chimeric**, for signal sequence of human serum **albumin** and desired protein, expression in yeast of, protein secretion in relation to)

IT Plasmid and Episome
(pNH008, **chimeric** human serum **albumin** signal peptide-**albumin** gene on, expression in Saccharomyces cerevisiae of, **albumin** secretion in relation to)

IT Peptides, biological studies
RL: BIOL (Biological study)
(signal, of human serum **albumin**, protein secretion from **recombinant** yeast using)

IT Gene and Genetic element, animal
(signal sequence, of human serum **albumin** gene, protein secretion from yeast in relation to)

IT **Interferons**
RL: PROC (Process)
(α , manufacture of, with yeast, human serum **albumin** signal peptide in)

IT **Interferons**
RL: PROC (Process)
(β , manufacture of, with yeast, human serum **albumin** signal peptide in)

IT **Interferons**
RL: PROC (Process)
(γ, manufacture of, with yeast, human serum **albumin** signal peptide in)

IT 125677-90-9P 125677-91-0P 125677-92-1P 125677-93-2P 125677-94-3P 125677-95-4P
RL: PREP (Preparation)
(human serum **albumin** signal peptide derivative, **recombinant** protein manufacture and secretion with yeast in relation to)

IT 125677-89-6P
RL: PREP (Preparation)
(human serum **albumin** signal peptide, **recombinant**

protein manufacture and secretion with yeast in relation to)
IT 9001-27-8P, Factor VIII 9002-72-6P, Growth hormone 9004-10-8P, Insulin, biological studies 9039-53-6P, Urokinase 11096-26-7P, Erythropoietin 62683-29-8P, Colony-stimulating factor 85637-73-6P, Atriopeptin
RL: IMF (Industrial manufacture); PREP (Preparation)
(manufacture and secretion of, with yeast, human serum **albumin** signal peptide in relation to)
IT 126115-99-9P
RL: PREP (Preparation)
(nucleotide sequence encoding human serum **albumin** signal peptide, **recombinant** protein manufacture and secretion with yeast in relation to)

L66 ANSWER 23 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1989:639534** HCAPLUS
DN **111:239534**
ED Entered STN: 23 Dec 1989
TI Pharmaceutical compositions containing **recombinant interferon-β**
IN Taforo, Terrance; Thomson, Jody; Shaked, Ze'ev; Hershenson, Susan; Thomson, James W.; Stewart, Tracy
PA Cetus Corp., USA
SO PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K047-00
ICS A61K045-02
CC 63-6 (Pharmaceuticals)
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8902750	A1	19890406	WO 1988-US3313	19880926 <--
	W: AU, DK, JP, NO				
	RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	US 5183746	A	19930202	US 1987-100679	19870929 <--
	AU 8825351	A1	19890418	AU 1988-25351	19880926 <--
PRAI	US 1987-100679		19870929 <--		
	US 1986-923423		19861027 <--		
	WO 1988-US3313		19880926 <--		

AB A stable parenteral composition in liquid or lyophilized form comprises a **recombinant interferon-β** (**IFN-**. **beta.**) protein dissolved in an inert carrier medium containing nonionic polymeric surfactants as a solubilizer/stabilizer. The surfactants include polyoxyethylene sorbitan fatty acid esters, a mixture of ethoxylated fatty alc. ethers and lauryl ether, ethoxylated octylphenol, a mixture of ethoxylated or propoxylated alcs., polyethylene glycol monooleate, ethoxylated phenol, and propylene oxide-ethylene oxide block copolymers. The composition further comprises addnl. bulking/stabilizing agents, such as dextrose. An **IFN-β** analog designated as **IFN-β** ser17 was recovered from Escherichia coli culture media and stabilized by adding 0.15% Trycol LAL-12 and pH was adjusted to 7.0 with NaOH. A bulking/stabilizing agent, i.e., 5% dextrose, was then added and the solution was sterile-filtered, aseptically filled into vials, and lyophilized. The **IFN-**. **beta.** formulations of this invention contain very low levels of aggregates and other potentially immunogenic characterisitcs and minimal or no strong solubilizing agents, such as SDS, and they are nontoxic and have good shelf life.
ST **interferon beta** surfactant solubilizer injection; lyophilization **interferon beta** stability
IT Solubilizers

Stabilizing agents
(nonionic surfactants and sugars as, for **interferon** β -containing parenteral compns.)

IT **Albumins, biological studies**
RL: BIOL (Biological study)
(parenteral **interferon-β** composition containing nonionic surfactants and, as stabilizer)

IT Carbohydrates and Sugars, biological studies
RL: BIOL (Biological study)
(parenteral **interferon-β** composition containing nonionic surfactants and, as stabilizers)

IT Surfactants
(nonionic, parenteral **interferon-β** composition containing, as stabilizers)

IT Pharmaceutical dosage forms
(parenterals, containing β **-interferons**, nonionic surfactants and sugars in, as solubilizers/stabilizers)

IT **Interferons**
RL: BIOL (Biological study)
(β , parenteral compns. containing, solubilizers/stabilizers for, nonionic surfactants and sugars as)

IT 50-70-4, Sorbitol, biological studies 50-99-7, Dextrose, biological studies 56-81-5, Glycerol, biological studies 69-65-8, Mannitol 87-89-8, Inositol 151-21-3, Sodium dodecyl sulfate, biological studies
RL: BIOL (Biological study)
(parenteral **interferon-β** composition containing nonionic surfactants and, as stabilizer)

IT 9002-92-0, Ethoxylated lauryl alcohol 9002-93-1, Triton X305 9004-78-8, Ethoxylated phenol 9004-96-0 9005-64-5, Polyoxyethylene sorbitan monolaurate 9005-65-6 9036-19-5, Ethoxylated octylphenol 12616-49-8, Plurafac C17 106392-12-5, Propylene oxide-ethylene oxide blocker copolymer
RL: BIOL (Biological study)
(parenteral **interferon-β** composition containing, as stabilizer)

L66 ANSWER 24 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1989:18548** HCAPLUS
DN **110:18548**
ED Entered STN: 21 Jan 1989
TI Method for treatment of essential (hemorrhagic) thrombocythemia with human α **-interferon**
IN Delwiche, Francis; Flament-Grivegnee, Jocelyn; Gangji, Diamond; Monsieur, Rita; Stryckmans, Pierre; Velu, Thierry; Wybran, Joseph
PA Boehringer Ingelheim International G.m.b.H., Fed. Rep. Ger.
SO U.S., 4 pp.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K045-02
NCL 424085000
CC 1-8 (Pharmacology)
Section cross-reference(s): 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4743445	A	19880510	US 1985-758729	19850725 <--
PRAI	US 1985-758729		19850725 <--		

AB Essential thrombocythemia is treated by administration of an effective amount of human α **-interferon.** Patients with essential thrombocythemia were given i.m. injections of 5 + 106 IU **recombinant** human **interferon-α** 2(Arg) (I)/day for 30 days. After 15 days, the dose was doubled if the results

of the treatment were insufficient. After 30 days, the same dose was given twice a week as a maintenance dose. In all patients the number of thrombocytes returned to normal. A parenteral formulation comprises I 5 + 106 IU, isotonic phosphate buffer (pH 7) q.s., human serum **albumin** 20.0 mg, and water for injection 1.0 mL.

ST essential thrombocythemia **alpha interferon**

IT Blood platelet
(α **-interferon** of human effect on)

IT Blood platelet
(disease, essential thrombocythemia, treatment of, with α **-interferon** of human)

IT **Interferons**
RL: BIOL (Biological study)
(α , essential thrombocythemia treatment with, of human)

IT 118104-04-4
RL: BIOL (Biological study)
(essential thrombocythemia treatment with)

L66 ANSWER 25 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1988:562850** HCAPLUS
DN **109:162850**
ED Entered STN: 12 Nov 1988
TI **Recombinant** human **interferon alpha**-2a: delivery to lymphoid tissue by selected modes of application
AU Supersaxo, Andreas; Hein, Wayne; Gallati, Harald; Steffen, Hans
CS Preclin. Dev., F. Hoffmann-La Roche und Co. Ltd., Basel, Switz.
SO Pharmaceutical Research (**1988**), 5(8), 472-6
CODEN: PHREEB; ISSN: 0724-8741
DT Journal
LA English
CC 1-2 (Pharmacology)
AB Following s.c. or injection device (i.d.) administration, **recombinant** human **interferon** α -2a (rIFN α-2a) of mol. weight 19,000 was absorbed mainly by the lymphatics. This results in high rIFN α-2a levels in the lymphoid tissue which drains the application site, while blood plasma levels are relatively low. The maximum measured concns. of rIFN α-2a in the efferent popliteal lymph varied by a factor of 105 between intradermal/s.c. and i.v. administration and was affected neither by the **infusion** rate nor by the coadministration of **albumin**. This may help to improve the mode of administration and therapeutic efficacy of protein drugs whose targets are lymphoid cells.

ST **interferon** α 2a delivery lymph gland

IT Lymphatic system
(**interferon** α -2a absorption by, after parenteral administrations)

IT **Albumins, biological studies**
RL: BIOL (Biological study)
(**interferon** α -2a delivery to lymphoid tissue in relation to)

IT Lymph gland
(**interferon** α -2a delivery to, parenteral administration routes for)

IT **Interferons**
RL: BIOL (Biological study)
(α **-2a**, delivery to lymphoid tissue of **recombinant**, parenteral administration routes for)

L66 ANSWER 26 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1987:583557** HCAPLUS
DN **107:183557**
ED Entered STN: 14 Nov 1987
TI Improved formulation for **recombinant** β -

interferon with protein or sugar stabilizer
IN Hanisch, Wolfgang Helmut; Taforo, Terrance; Fernandes, Peter Michael
PA Cetus Corp., USA
SO Eur. Pat. Appl., 34 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM A61K045-02
ICS A61K047-00; C07K003-02; C12P021-02
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 3
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 215658	A2	19870325	EP 1986-307070	19860912 <--
	EP 215658	A3	19890208		
	EP 215658	B1	19940601		
	R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
	US 4992271	A	19910212	US 1985-775751	19850913 <--
	AT 106247	E	19940615	AT 1986-307070	19860912 <--
PRAI	US 1985-775751		19850913 <--		
	US 1982-422421		19820923 <--		
	US 1983-495896		19830518 <--		
	US 1984-592077		19840323 <--		
	US 1985-752403		19850705 <--		
	EP 1986-307070		19860912 <--		

AB **Recombinant** β-human **interferon** (**.beta** .-HIFN) is dissolved in a non-toxic, inert, therapeutically compatible aqueous carrier, at a pH of 2-4. The solution contains a stabilizer for the β-HIFN, particularly human plasma protein fraction, human serum **albumin**, or mannitol. This formulation results in very low sodium dodecyl sulfate levels. β -**Interferon** 0.25 mg/mL was formulated using 2.5% plasma protein fraction at pH 3-4, incubated 15-45 min.; the pH was adjusted to 7.3-7.5. At this pH, the solns. were very clear. The use of 5.0% human serum **albumin** also gave clear solns., whereas 2.5% HSA resulted in slightly hazy solns.
ST **interferon** formulation protein solubilization; stabilizer **recombinant beta interferon**
IT **Albumins, biological studies**
RL: BIOL (Biological study)
(human, stabilizer for **recombinant** β-human **interferon**)
IT Proteins, specific or class, biological studies
RL: BIOL (Biological study)
(of blood plasma, as stabilizer for **recombinant** β-human **interferon**)
IT **Recombination**, genetic
(of β -**interferon**, purification and formulation for)
IT **Interferons**
(β -, **recombinant**, stabilization of, in formulation)
IT 151-21-3, Sodium dodecyl sulfate, biological studies
RL: PRP (Properties)
(reduced levels of, in formulations of β -**interferon**)
IT 50-99-7, Dextrose, biological studies 69-65-8, Mannitol
RL: BIOL (Biological study)
(stabilizer, for **recombinant** β -**interferon**-containing pharmaceutical composition)

L66 ANSWER 27 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1987:464710** HCAPLUS
DN **107:64710**

ED Entered STN: 21 Aug 1987
TI Potency stability of **recombinant** (serine-17) human **interferon-β**
AU Geigert, John; Ziegler, Diana L.; Panschar, Barbara M.; Creasey, Abla A.; Vitt, Charles R.
CS Dep. Tech. Dev., Cetus Corp., Emeryville, CA, 94608, USA
SO Journal of Interferon Research (**1987**), 7(2), 203-11
CODEN: JIREDJ; ISSN: 0197-8357
DT Journal
LA English
CC 63-3 (Pharmaceuticals)
AB The antiviral activity of Escherichia coli-derived (serine-17) human **interferon-β** , formulated with human serum **albumin**, is stable for 2 yr when lyophilized and stored under refrigeration. This product shows an Arrhenius line fit for the stability of its activity when tested at multiple isothermal temps. (25-80°). In both isothermal and non-isothermal elevated temperature studies, increasing the level of human serum **albumin** in the formulation results in increased thermal stability.
ST **interferon** serine 17 **recombinant** formulation stability
IT Kinetics of decomposition
(of **recombinant** human β **-interferon** in **albumin** formulation)
IT **Albumins, uses and miscellaneous**
RL: USES (Uses)
(β **-interferon recombinant** serine-17 stabilization by formulation with human)
IT **Interferons**
(β -, stability of **recombinant** serine-17, in human serum **albumin** formulation)

L66 ANSWER 28 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1986:174635** HCAPLUS
DN **104:174635**
ED Entered STN: 17 May 1986
TI **Interferon** solubilization with amino acids
IN Kato, Yasuki; Hayakawa, Eiji; Furuya, Kunitoshi; Kondo, Akira
PA Kyowa Hakko Kogyo Co., Ltd. , Japan
SO Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM A61K045-02
CC 63-3 (Pharmaceuticals)
Section cross-reference(s): 15
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 163111	A2	19851204	EP 1985-104849	19850422 <--
	EP 163111	A3	19870930		
	EP 163111	B1	19901003		
	R: DE, FR, GB, IT				
	JP 60243028	A2	19851203	JP 1984-86972	19840428 <--
	JP 05058000	B4	19930825		
	CA 1264665	A1	19900123	CA 1985-479841	19850423 <--
	US 4675183	A	19870623	US 1985-726971	19850425 <--
PRAI	JP 1984-86972		19840428 <--		

AB **Interferon** is solubilized by addition of 5 + 10-6 - 5 + 10-3 mol amino acid/106 units **interferon.** The amino acid may be arginine, histidine, lysine, hydroxylysine, ornithine, glutamine, γ-aminobutyric acid, ε-aminocaproic acid, or a salt of these compds. Thus, 5 mg serum **albumin**, 5 mg NaCl, 30 mg arginine-HCl, and 3 + 106 units of γ- **interferon** were

mixed with 2 mL H2O, and freeze-dried. The product was dissolved in 5 mL H2O, held 6 h at 25°, and the absorbance was measured at 400 nm. The amount of γ- **interferon** that remained in solution was 98%. This solubilization may be used to facilitate the isolation and purification of **interferon** produced by **recombinant** DNA technol.

ST **interferon** solubilizer amino acid; arginine **interferon** solubilization

IT Solubilizers
(amino acids, for **interferon**)

IT Amino acids, uses and miscellaneous
RL: PRP (Properties)
(**interferons** solubilization by)

IT **Interferons**
(α -, solubilization of, with amino acids)

IT **Interferons**
(β -, solubilization of, with amino acids)

IT **Interferons**
(γ-, solubilization of, with amino acids)

IT 56-85-9, properties 56-87-1, properties 60-32-2 70-26-8 71-00-1, properties 74-79-3, properties 657-27-2 1119-34-2 1190-94-9 2835-81-6 60259-81-6
RL: PRP (Properties)
(**interferons** solubilization by)

L66 ANSWER 29 OF 29 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1986:86802** HCAPLUS
DN **104:86802**
ED Entered STN: 22 Mar 1986
TI The lymphatic route - II. Pharmacokinetics of human **recombinant interferon**-α 2 injected with **albumin** as a retarder in rabbits
AU Bocci, Velio; Muscettola, Michela; Naldini, Antonella; Bianchi, Enrica; Segre, Giorgio
CS Inst. Gen. Physiol., Univ. Siena, Siena, 53100, Italy
SO General Pharmacology (**1986**), 17(1), 93-6
CODEN: GEPHDP; ISSN: 0306-3623
DT Journal
LA English
CC 15-5 (Immunochemistry)
AB An investigation was conducted to define whether multisite s.c. administration in unanesthetized, unrestrained rabbits of human **recombinant interferon**-α 2 (rec. **IFN**-α 2) either in saline, human **albumin** (ALB) solution (4, 7, and 10% final concns.), or in a solution containing 75 units of hyaluronidase, modified the pharmacokinetic parameters calculated from the IFN plasma level. Plasma disappearance rates of rec. **IFN**-**alpha**.2 were measured in rabbits after i.v. administration and the kinetics was adequately represented by a 3-compartment mammillary model. This model was the basis for evaluating the absorption and distribution of rec. **IFN**-α 2 after s.c. administration. The increase of ALB concentration (from 4 to 10%) caused a significant reduction of the plasma IFN maximum clearance, while both the mean residence time and the release time of IFN increased linearly with the ALB concentration The data support the postulation that s.c. administration of **albumin** acts as an interstitial fluid expander and may favor absorption of IFN via lymphatics rather than blood capillaries. Improvement of therapeutic index of IFN by using this route remains to be shown in clin. trials.

ST **interferon alpha** pharmacokinetics **albumin**

IT Lymphatic system
(**albumin** effect on **recombinant** α2-**interferon** pharmacokinetics in relation to, of humans and laboratory

animals)
IT Blood plasma
(α2- **interferon** pharmacokinetics in, **albumin**
effect on, in humans and laboratory animals)
IT **Albumins**
RL: BIOL (Biological study)
(α2- **interferon** pharmacokinetics response to, of humans
and laboratory animals)
IT **Interferons**
RL: BIOL (Biological study)
(α **2-**, pharmacokinetics of **recombinant**
, **albumin** effect on, of humans and laboratory animals)

=> => fil wpix
FILE 'WPIX' ENTERED AT 16:25:05 ON 02 FEB 2004
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FILE LAST UPDATED: 28 JAN 2004 <20040128/UP>
MOST RECENT DERWENT UPDATE: 200407 <200407/DW>
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DERWENT UPDATE 200403.
THE TIME RANGE CODE WILL ALSO CHANGE FROM 018 TO 2004.
SDIS USING THE TIME RANGE CODE WILL NEED TO BE UPDATED.
FOR FURTHER DETAILS: http://thomsonderwent.com/chem/polymers/ <<<

=> d all abeq tech abex tot

L88 ANSWER 1 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN **2003-421048** [39] WPIX
DNC **C2003-110745**
TI New hybrid polypeptide, useful for sequestering and/or purifying a
polypeptide of interest.
DC B04 D16
IN THOMAS, T; TILLETT, D
PA (PROT-N) PROTIGENE PTY LTD
CYC 101
PI WO 2003018616 A1 20030306 (200339)* EN 66p C07K001-14
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU
MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

ADT WO 2003018616 A1 WO 2002-AU1159 20020827

PRAI AU 2001-7298 20010827

IC ICM C07K001-14

ICS C07K001-36; **C07K019-00**; C12N009-00; C12N015-63

AB WO2003018616 A UPAB: 20030619

NOVELTY - A hybrid polypeptide comprises a polypeptide of interest linked to a polymerizable polypeptide, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) sequestering and/or purifying a polypeptide of interest;

(2) a hybrid nucleic acid comprising a nucleic acid encoding the hybrid polypeptide;

(3) a library comprising several hybrid nucleic acids, polypeptides or vectors;

(4) a vector comprising the hybrid nucleic acid;

(5) a cell transformed or transfected with the hybrid nucleic acid or vector; and

(6) purifying a polypeptide of interest.

USE - The hybrid polypeptide is useful for sequestering and/or purifying a polypeptide of interest (claimed).

Dwg.0/9

FS CPI

FA AB; DCN

MC CPI: B04-B04C; **B04-C01**; B04-E08; B04-F0100E; B04-G01; B04-H01; B04-H02B; B04-H04; **B04-H05**; B04-H19; B04-J01; B04-J02; B04-J05; B04-J10; B04-L04; B04-L05; B04-L06; B04-L07; B04-N03; B04-N04; B04-N06; B04-N08; B11-B; D05-C11; D05-H12A; D05-H12E; D05-H13; D05-H14; D05-H17C

TECH UPTX: 20030619

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Polypeptide: The hybrid polypeptide is produced in vivo. It is linked to a support, comprising the polymerizable polypeptide. The support polymerizable polypeptide comprises a polymerizable polypeptide identical to the hybrid polypeptide, or its variant. The polypeptide of interest is linked to the polymerizable polypeptide by fusing the polypeptide of interest directly to the polymerizable polypeptide or by a linker polypeptide. It is prokaryotic or eukaryotic in origin. It is a synthetic polypeptide. It comprises endonuclease, a methylase, an oxidoreductase, a transferase, a hydrolase, a lysase, an isomerase, a ligase, a storage polypeptide, a fertitin, an **ovalbumin**, a transport protein, hemoglobin, serum **albumin** or ceruloplasmin, an antigen, an antigenic determinant for use in the preparation of vaccines or diagnostic agents, a protective protein, a defense protein, thrombin, fibrinogen, binding proteins, antibodies, immunoglobulins, a human growth hormone, somatostatin, prolactin, estrange, progesterone, melanocyte, thyrotropin, calcitonin, gonadotropin, insulin, a hormone identified as being involved in the immune system, interleukin 1, interleukin 2, colony simulating factor, macrophage-activating factor, interferon, a structur al element, collagen, elastin, alpha-keratin, glyco-protein, virus-protein and muca-protein. The linker polypeptide comprises a recognition site for a proteolytic agent and a multiple cloning site. It also comprises a spacer polypeptide of sufficient length to allow or enhance cleavage of the polypeptide of interest from the polymerizable polypeptide, or to avoid unfavorable steric interference between the polypeptide of interest and the polymerizable polypeptide.

The recognition site comprises an amino acid sequence consisting of:

(a) Leu-Glu-VaI-Leu-Phe-Gln-Gly-Pro;

(b) Leu-Val-Pro-Arg-Gly-Ser;

(c) Ile-Glu-Gly-Arg; or
(d) Asp-Asp-Asp-Asp-Lys.
The chemical capable of proteolytic activity is cyanogen bromide. The polypeptides are linked by antibody interaction, which is achieved by:
(a) attaching an antibody specific for the polypeptide of interest to the polymerizable polypeptide; or
(b) using a bi-specific antibody directed to both the polypeptide of interest and the polymerizable polypeptide.
The polymerizable polypeptide is a polypeptide that naturally polymerizes with itself. It is tubulin or actin. It is an FtsZ or Escherichia coli FtsZ protein or its variant. The variant Escherichia coli FtsZ protein comprises replacement of the aspartate residue at position 212 of the protein with a cysteine or asparagine residue. The variant FtsZ protein comprises a mutation selected from replacement of alanine by threonine at position 70, replacement of aspartate by alanine at position 209 or replacement of aspartate by alanine at position 269. The polymerizable polypeptide requires an intermediary polypeptide or other molecule in order to polymerize.
Preferred Method: Sequestering and/or purifying a polypeptide of interest comprises polymerizing the hybrid polypeptide under controlled chemical and/or physical conditions. It is polymerized by a change in temperature and by the addition of an agent that induces polymerization. The polymerization inducing agent is GTP, ATP and/or a cation. The cation comprises magnesium, calcium, nickel, cobalt, zinc or manganese. The polymerized hybrid polypeptide is purified by a first purification step, which may be the only purification step or may be followed by further purification steps. The first purification step purifies the polymerized hybrid polypeptide by physical techniques discriminating on the basis of size and/or weight. The polymerized hybrid polypeptide is also purified by centrifugation, differential sedimentation, filtration, dialysis and/or flow sorting, where the polymerized hybrid polypeptide is isolated. After the first purification step the polymerized hybrid polypeptide is dissociated. The dissociation is achieved by removal of the agent which induces polymerization and/or incubation of the polymerized hybrid polypeptide at a suitable temperature. The dissociated hybrid polypeptide is purified by a second purification step, which comprises purification of the hybrid polypeptide on the basis of size and/or weight. The polymerization, dissociation and purification of the polymerizable hybrid polypeptide are repeated so that substances larger and smaller than the hybrid polypeptide are removed. The polymerizable polypeptide is cleaved from the polypeptide of interest by a proteolytic agent, which does not substantially interfere with the biological or chemical activity of the polypeptide of interest or the polymerizable polypeptide. After the cleavage of the polypeptide of interest from the polymerizable polypeptide, the protease hybrid polypeptide is polymerized. The proteolytic agent comprises 3C-protease from a human rhinovirus type 14 (HRV protease 3C), thrombin, Factor Xa, enterokinase and a chemical capable of proteolytic activity. It is linked to a polymerizable polypeptide to form a protease hybrid polypeptide. The polymerizable polypeptide to which the protease is linked is identical to the polymerizable polypeptide to which the polypeptide of interest is linked, or is a variant of it.
Purifying a polypeptide of interest comprises:
(a) expressing the hybrid nucleic acid in a cell to produce a hybrid polypeptide comprising the polypeptide of interest and a polymerizable polypeptide;
(b) polymerizing the hybrid polypeptide;
(c) purifying the polymerized hybrid polypeptide;
(d) cleaving the polypeptide of interest from the polymerizable polypeptide; and
(e) purifying the polypeptide of interest.
ABEX UPTX: 20030619
EXAMPLE - No suitable example given.

L88 ANSWER 2 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN **2002-179329** [23] WPIX
CR 2001-602931 [68]
DNC **C2002-055553**
TI New **albumin** fusion proteins with extended shelf life, useful for treating leukemia, warts, hepatitis, multiple sclerosis and AIDS, comprises therapeutic protein fused to **albumin**.
DC B04 D16
IN BALLANCE, D J; PRIOR, C P; SADEGHI, H; SLEEP, D; TURNER, A J
PA (DELZ) DELTA BIOTECHNOLOGY LTD; (PRIN-N) PRINCIPIA PHARM CORP; (BALL-I) BALLANCE D J; (PRIO-I) PRIOR C P; (SADE-I) SADEGHI H; (SLEE-I) SLEEP D; (TURN-I) TURNER A J
CYC 96
PI WO 2001079271 A1 20011025 (200223)* EN 294p C07K014-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001061024 A 20011030 (200225) C07K014-00
EP 1278767 A1 20030129 (200310) EN C07K014-00
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
US 2003199043 A1 20031023 (200370) C12P021-02
JP 2003530839 W 20031021 (200373) 453p C12N015-09
ADT WO 2001079271 A1 WO 2001-US12009 20010412; AU 2001061024 A AU 2001-61024 20010412; EP 1278767 A1 EP 2001-934875 20010412, WO 2001-US12009 20010412; US 2003199043 A1 Provisional US 2000-229358P 20000412, Provisional US 2000-199384P 20000425, Provisional US 2000-256931P 20001221, US 2001-832501 20010412; JP 2003530839 W JP 2001-576866 20010412, WO 2001-US12009 20010412
FDT AU 2001061024 A Based on WO 2001079271; EP 1278767 A1 Based on WO 2001079271; JP 2003530839 W Based on WO 2001079271
PRAI US 2000-256931P 20001221; US 2000-229358P 20000412; US 2000-199384P 20000425; US 2001-832501 20010412
IC ICM C07K014-00; C12N015-09; C12P021-02
ICS A61K038-00; A61K038-16; **A61K038-21**; A61K038-43; A61K038-46; A61K038-48; A61K038-55; A61K039-395; A61K047-48; A61P001-16; A61P015-00; A61P017-12; A61P025-28; A61P031-12; A61P031-14; A61P031-18; A61P031-20; A61P035-00; A61P035-02; C07H021-04; **C07K014-52**; **C07K014-56**; C07K014-745; C07K014-75; **C07K014-76**; **C07K014-765**; C07K014-81; C07K016-00; **C07K019-00**; C12N001-19; C12N001-21; C12N005-06; C12N005-10; C12N009-14; C12N009-74; C12N009-99; C12N015-00
AB WO 200179271 A UPAB: 20031112
NOVELTY - An **albumin** fusion protein (I) comprising:
(a) a therapeutic protein (X) and **albumin** (A) containing a fully defined sequence (S1) of 585 amino acids as given in the specification;
(b) X and a fragment or variants of S1, where the fragment or variants has **albumin** activity; or
(c) a fragment or variant of X and A, where the fragment or variant has a biological activity of X, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) an **albumin** fusion protein (II) comprising a peptide inserted into A comprising amino acids 54-61, 76-89, 92-100, 170-176, 247-252, 266-277, 280-288, 362-368, 439-447, 462-475, 478-486 or 560-566 of S1;
(2) an **albumin** fusion protein (III) comprising a single chain antibody or its portion and A or its fragment or variant;

(3) a composition comprising any of (I)-(III) and a pharmaceutically active carrier;

(4) a kit comprising the composition;

(5) treating a disease or disorder that is modulated by X in a patient comprising administering any of (I)-(III);

(6) extending the shelf life of X comprising fusing X or its fragment or variant to A or its fragment or variant, sufficient to extend the shelf-life of X compared to the shelf life of X in an unfused state;

(7) a nucleic acid molecule (IV) comprising a polynucleotide sequence encoding any of (I)-(III);

(8) a vector comprising (IV); and

(9) a host cell comprising (IV).

ACTIVITY - Cytostatic; dermatological; virucide; anti-HIV; neuroprotective; hepatotropic; antiinflammatory. Tests are described but no results are given in the source material.

MECHANISM OF ACTION - Gene therapy.

USE - The fusion protein is useful for the treatment of hairy cell leukemia, Kaposi's sarcoma, genital warts, anal warts, chronic hepatitis B, chronic non-A, non-B hepatitis, hepatitis C/D, chronic myelogenous leukemia, renal cell carcinoma, bladder carcinoma, ovarian carcinoma, cervical carcinoma, skin cancer, recurrent respirator papillomatosis, non-Hodgkin's lymphoma, cutaneous T-cell lymphoma, melanoma, multiple myeloma, acquired immunodeficiency syndrome (AIDS), multiple sclerosis and glioblastoma. The fusion of **albumin** extends the shelf life and the in vivo and in vitro biological activity of the therapeutic protein (all claimed).

ADVANTAGE - Therapeutic proteins can be stabilized to extend shelf life and/or retain the protein's activity for extended periods of time in solution, in vivo or in vitro by genetically or chemically fusing the protein to **albumin** or its fragment or variant. In addition the use of **albumin** fusion proteins reduces the need to formulate protein solutions with large excesses of carrier proteins to prevent loss of therapeutic protein due to factors such as binding to the container. The extension of shelf life was tested by measuring biological activity (Nb2 cell proliferation) of human **albumin**-human growth hormone (HA-hGH) fusion protein remaining after incubation in cell culture media for up to 3 weeks at 37 deg. C. At week 3 there was still approx. 95% cell proliferation compared to no activity of unfused hGH (no observed activity by week 2).

Dwg.0/18

FS CPI

FA AB; DCN

MC CPI: **B04-C01G**; B04-E02H; B04-E08; B04-F0100E; B04-G01; **B04-H05A**; B04-H19; B04-L05A; **B04-N02A**; B04-N08; B14-A02A; B14-A02B1; B14-G01B; B14-H01; B14-N12; B14-N17; B14-S01; B14-S03A; D05-C12; D05-H12C; D05-H12E; D05-H14; D05-H17C

TECH UPTX: 20020411

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: The fusion proteins can be prepared by standard recombinant techniques.

Preferred Fusion Protein: **Albumin** activity is the ability to prolong the shelf life of X compared to the shelf life of X in an unfused state. Preferably the fragment or variant of (I) comprises amino acids 1-387 of S1. X is chosen from serum cholinesterase, alpha-1 antitrypsin, aprotinin, coagulated complex, von Willebrand factor, fibrinogen, factor VII, factor VIIA activated factor, factor VIII, factor IX, factor X, factor XIII, c1 inactivator, antithrombin III, thrombin, prothrombin, apo-lipoprotein, c-reactive protein, protein C, immunoglobulin and preferably interferon (IFN)-alpha. X or its fragment or variant is fused to the N or C-terminus of A. (I)-(III) comprises a first and second X, where the first X is different from the second X. X is separated from A by a linker. The fusion protein has the formula R1-L-R2, R2-L-R1 or R1-L-R2-L-R1, where:

R1 = X

L = peptide linker; and
R2 = A or its fragment or variant.
The in vitro or in vivo activity of X fused to A is greater than the in vitro or in vivo biological activity of X in an unfused state. The protein is expressed in a glycosylation and protease deficient yeast. Alternatively it is expressed by a mammalian cell in culture. The fusion protein further comprises a secretion leader sequence.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: The fusion proteins can be produced by standard chemical synthetic techniques.

ABEX UPTX: 20020411

ADMINISTRATION - 1 microgram/kg/day to 10 mg/kg/day, preferably 0.01-1 mg/kg/day of **albumin** fusion proteins are administered by standard routes.

EXAMPLE - A human **albumin**-human growth hormone (HA-hGH) fusion protein was prepared. The hGH cDNA was obtained from a human pituitary gland cDNA library by polymerase chain reaction (PCR) amplification. The PCR product was purified and then digested with EcoR1 and HindIII. After further purification of the EcoR1-HindIII fragment by gel electrophoresis, the product was cloned into pUC19 digested with EcoR1 and HindIII to give pHGH1. The polylinker sequence of the phagemid pBluescribe (+) (Stratagene) was replaced by inserting an oligonucleotide linker formed by annealing 2 75-mer oligonucleotides between the EcoR1 and HindIII sites to form pBST(+). The new polylinker included a unique NotI site. the NotI HA expression cassette of pAYE309 comprising the PRBI promoter, DNA encoding the HA/MFalpha-1 hybrid leader sequence, DNA encoding HA and the ADH1 terminator, was transferred to pBST(+) to form pHA1. The HA sequence was removed from this plasmid by digestion with HindIII followed by religation to form pHA2. Cloning of the hGH cDNA provided the hGH coding region lacking the pro-hGH sequence and the first 8 base pairs (bp) of the mature hGH sequence. In order to construct an expression plasmid for secretion of hGH from yeast, a yeast promoter, signal peptide and the first bp of the hGH sequence were attached to the 5' end of the cloned hGH sequence. The HindIII-SfaNI fragment from pHA1 was attached to the 5' end of the EcoR1/HindIII fragment from pHGHI via 2 synthetic oligonucleotides to generate a double stranded fragment of DNA with sticky ends that can anneal with SfaNI and EcoR1 sticky ends. The HindIII fragment formed was cloned into HindIII digested pHA2 to make pHGH2 such that the hGH cDNA was positioned downstream of the PRBI promoter and HA/MFalpha-1 fusion leader sequence. The NotI expression cassette contained in pHGH2 was cloned into the NotI-digested pSAC35 to make pHGH12. This plasmid comprised the entire 2 micro m plasmid to provide replication functions and the LEU2 gene for selection of transformants. pHGH12 was introduced into S. cerevisiae D88 by transformation and individual transformants were grown for 3 days at 30 degrees C in 10 mL YEPD (1% w/v yeast extract, 2% w/v peptone, 2% w/v dextrose). After centrifugation of the cells, the supernatants were examined by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) and were found to contain protein which was of the expected size and recognized by anti-hGHG antiserum on Western blots.

L88 ANSWER 3 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN **2001-616754** [71] WPIX
CR 2001-602931 [68]; 2001-611723 [70]; 2001-616755 [71]; 2001-616756 [71]; 2002-010886 [01]; 2003-810996 [76]; 2004-033644 [03]
DNC **C2001-184720**
TI **Albumin** fusion proteins comprising a therapeutic protein and **albumin**, useful in the treating immune system disorders (e.g. transplant rejection), blood related disorders (e.g. myocardial infarction) and hyperproliferative disorders.
DC B04 D16
IN **HASELTINE, W A; ROSEN, C A**
PA (HUMA-N) HUMAN GENOME SCI INC
CYC 96

PI WO 2001079443 A2 20011025 (200171)* EN 365p C12N000-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001059063 A 20011030 (200219) C12N000-00
EP 1274719 A2 20030115 (200313) EN C07K001-00
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
JP 2003530846 W 20031021 (200373) 469p C12N015-09

ADT WO 2001079443 A2 WO 2001-US11924 20010412; AU 2001059063 A AU 2001-59063 20010412; EP 1274719 A2 EP 2001-932546 20010412, WO 2001-US11924 20010412; JP 2003530846 W JP 2001-577427 20010412, WO 2001-US11924 20010412

FDT AU 2001059063 A Based on WO 2001079443; EP 1274719 A2 Based on WO 2001079443; JP 2003530846 W Based on WO 2001079443

PRAI US 2000-256931P 20001221; US 2000-229358P 20000412; US 2000-199384P 20000425

IC ICM C07K001-00; C12N000-00; C12N015-09
ICS A01N037-18; A61K038-00; **A61K038-21**; A61K038-28; A61K039-395; A61K047-48; A61K048-00; A61P001-16; A61P013-00; A61P025-00; A61P031-14; A61P031-18; A61P031-20; A61P035-00; A61P035-02; C07K014-47; **C07K014-76**; **C07K019-00**; C12N001-19; C12N005-10

AB WO 200179443 A UPAB: 20040112
NOVELTY - **Albumin** fusion proteins (P1) comprising a therapeutic protein (T1) (or its fragment or variant having the activity of T1) and **albumin** comprising the 585 amino acid sequence (I) defined in the specification (or its fragment or variant having **albumin** activity), are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a kit comprising a composition containing P1;

(2) a method of treating a disease or disorder, preferably modulated by T1, in a patient, comprising administering P1;

(3) a method of extending the shelf-life of T1, comprising fusing T1 or its fragment or variant, to **albumin** or its fragment or variant, where the shelf-life of T1 or its fragment or variant as part of a fused protein is extended when compared to T1 or its fragment or variant in an unfused state;

(4) a nucleic acid (N1) comprising a nucleotide sequence encoding P1;

(5) a vector comprising N1; and

(6) a host cell comprising N1.

ACTIVITY - Cytostatic; antiinflammatory; antileukemic; antiarthritic; antirheumatic; immunosuppressive; cardiant; nootropic; neuroprotective; antimicrobial; vulnerary.

To test whether sympathetic neuronal cell viability is supported by an **albumin** fusion protein, the chicken embryo neuronal survival assay (Senaldi, et al., Proc. Natl. Acad., Sci., U.S.A, 96:11458-63 (1998)). Briefly, motor and sympathetic neurons were isolated from chicken embryos, resuspended in L15 medium (with 10% foetal calf serum (FCS), glucose, sodium selenite, progesterone, **conalbumin**, putrescine and insulin) and Dulbecco's modified Eagles medium (with 10% FCS, glutamine, penicillin, and 25 mM Hepes buffer (pH 7.2)), respectively and incubated at 37 degrees Centigrade in 5% carbon-dioxide in the presence of different concentrations of the purified fusion protein, as well as negative control lacking any cytokine, After 3 days, neuronal survival was determined by evaluation of cellular morphology, and through the use of the colorimetric assay of Mosmann (Mosmann, T., J. Immunol., Methods, 65:55-63 (1983)). Enhanced neuronal cell viability as compared to the controls lacking cytokine is indicative of the ability of the **albumin** fusion protein to enhance the survival of neuronal cells.

MECHANISM OF ACTION - Gene therapy.

USE - The **albumin** fusion proteins are also useful in the treatment, prevention, diagnosis, and/or detection of diseases, disorders such as immune system disorders (e.g. transplant rejection), blood related disorders (e.g. myocardial infarction), hyperproliferative disorders (e.g. childhood acute myeloid leukemia), renal disorders (e.g. glomerulonephritis), cardiovascular disorders (e.g. arrhythmias), respiratory disorders (e.g. non-allergic rhinitis), neurological diseases (e.g. Alzheimer's disease), endocrine disorders (e.g. pheocytochroma), reproductive system disorders (e.g. syphilis), infectious diseases (e.g. measles), gastrointestinal disorders (e.g. irritable bowel syndrome) and wound healing.

Dwg.0/15

FS CPI

FA AB; DCN

MC CPI: **B04-C01**; B04-E02F; B04-E08; B04-F0100E; B04-F0200E; B04-F0900E; B04-F1100E; **B04-N02A0E**; B14-A01; B14-A02; B14-D01; B14-E10; B14-F01; B14-F02; B14-G01; B14-G02; B14-G03; B14-H01; B14-J01; B14-K01; B14-N10; B14-N17B; B14-S03; **D05-H12B2**; D05-H12E; D05-H14A2; D05-H14B2

TECH UPTX: 20011203

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Fusion Protein: The **albumin** activity is the ability to prolong the shelf-life of T1 compared to the shelf-life of T1 in an unfused state. The **albumin** fragment or variant comprises amino acids 1-387 of (I).

T1 or its fragment or variant is fused to the C-terminal of the **albumin** or the C-terminus of the fragment or variant of **albumin**. Alternatively, T1 or its fragment or variant is fused to the N-terminal of the **albumin** or the N-terminus of the fragment or variant of **albumin**. Alternatively, T1 or its fragment or variant is fused to the N-terminus and C-terminus of the **albumin** , or the N-terminus and C-terminus of the fragment or variant of **albumin**.

P1 comprises a first T1 or its fragment or variant, and a second T1 or its fragment or variant, where the first T1 is different from the second T1. T1 or its fragment or variant is separated from the **albumin** or the fragment or variant of **albumin** by a linker. Preferably, P1 is of the formula (S1), (S2) or (S3).

R1-L-R2 (S1);

R2-L-R1 (S2); or

R1-L-R2-L-R1 (S3).

Where

R1 = is T1 or its fragment or variant;

L = is a peptide linker; and

R2 = is **albumin** comprising the sequence of (I), or its fragment or variant.

The shelf-life of the **albumin** fusion protein is greater than the shelf-life of T1 or its fragment or variant in an unfused state. The in vitro or in vivo biological activity of T1 or its fragment or variant, fused to **albumin** or its fragment or variant, is greater than the in vitro or in vivo, respectively, biological activity of T1 or its fragment or variant, in an unfused state.

Alternatively, P1 comprises T1 or its fragment or variant, inserted into an **albumin** comprising the sequence of (I) or its fragment or variant. Preferably, the **albumin** comprises residues 54-61, 76-89, 92-100, 170-176, 247-252, 266-277, 280-288, 362-368, 439-447, 462-475, 478-486, or 560-566 of (I). The portion of **albumin** is sufficient to prolong the shelf-life of T1, or its fragment or variant, as compared to the shelf-life of T1, or its fragment or variant in an unfused state.

The portion of **albumin** is sufficient to prolong the in vitro and in vivo biological activity of T1 or its fragment or variant, as compared to the in vitro and in vivo biological activity of T1 or its fragment or

variant, in an unfused state.
P1 is non-glycosylated and is expressed in yeast which is glycosylation deficient. The yeast may also be protease deficient. Alternatively, P1 is expressed by a mammalian cell in culture. P1 further comprises a secretion leader sequence.

ABEX UPTX: 20011203
ADMINISTRATION - The **albumin** fusion proteins can be administered orally, rectally, parenterally, intracisternally, intravaginally, intraperitoneally, topically, bucally, or as an oral or nasal spray. The dosage is 1 microgram/kg/day to 10 mg/kg/day, preferably 0.01 to 1, mg/kd/day. If given continuously, the **albumin** fusion protein is typically administered at a dose rate of 1-50 micrograms/kg/hour, either by 1-4 injections per day or by continuous subcutaneous infusions.

L88 ANSWER 4 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN **2001-611723** [70] WPIX
CR 2001-602931 [68]; 2001-616754 [71]; 2001-616755 [71]; 2001-616756 [71]; 2002-010886 [01]; 2003-810996 [76]; 2004-033644 [03]
DNC **C2001-182838**
TI New **albumin** fusion proteins, useful for treating diseases and disorders such as cancer, comprise therapeutic protein fused to **albumin**.
DC B04 D16
IN **HASELTINE, W A; ROSEN, C A**
PA (HUMA-N) HUMAN GENOME SCI INC
CYC 96
PI WO 2001079442 A2 20011025 (200170)* EN 362p C12N000-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001064563 A 20011030 (200219) C12N000-00
EP 1276849 A2 20030122 (200315) EN C12N001-18
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
JP 2003531590 W 20031028 (200373) 540p C12N015-09
ADT WO 2001079442 A2 WO 2001-US11850 20010412; AU 2001064563 A AU 2001-64563 20010412; EP 1276849 A2 EP 2001-938994 20010412, WO 2001-US11850 20010412; JP 2003531590 W JP 2001-577426 20010412, WO 2001-US11850 20010412
FDT AU 2001064563 A Based on WO 2001079442; EP 1276849 A2 Based on WO 2001079442; JP 2003531590 W Based on WO 2001079442
PRAI US 2000-256931P 20001221; US 2000-229358P 20000412; US 2000-199384P 20000425
IC ICM C12N000-00; C12N001-18; C12N015-09
ICS A61K038-00; **A61K038-21**; A61K039-395; A61K048-00; A61P001-04; A61P001-16; A61P001-18; A61P003-10; A61P005-14; A61P005-40; A61P007-04; A61P007-06; A61P009-00; A61P009-06; A61P009-10; A61P009-12; A61P011-00; A61P011-06; A61P013-00; A61P013-02; A61P013-08; A61P013-12; A61P015-00; A61P015-10; A61P015-18; A61P017-00; A61P017-02; A61P019-00; A61P019-02; A61P019-08; **A61P021-00**; A61P021-04; A61P025-00; A61P025-08; A61P025-16; A61P025-28; A61P027-02; A61P029-00; A61P031-00; A61P031-12; A61P031-16; A61P031-18; A61P031-22; A61P033-02; A61P033-06; A61P033-12; A61P035-00; A61P035-02; A61P037-00; A61P037-08; A61P039-02; A61P041-00; A61P043-00; C07K014-47; C07K014-76; C07K019-00; C12N001-19; C12N005-10
AB WO 200179442 A UPAB: 20040112
NOVELTY - An **albumin** fusion protein (I) comprising a therapeutic protein: X and (a fragment or variant of) **albumin** comprising a fully defined sequence (S18) of 585 amino acids as given in the specification, (where the fragment or variant has **albumin** or

therapeutic protein: X activity) is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a kit comprising a composition containing (I);

(2) treating a disease or disorder (that is modulated by therapeutic protein: X or its fragment or variant) comprising administering (I);

(3) extending the shelf life of therapeutic protein: X comprising fusing therapeutic protein: X or its fragment or variant to **albumin** or its fragment or variant, sufficient to extend the shelf life of therapeutic protein: X compared to the shelf life of therapeutic protein: X in an unfused state;

(4) a nucleic acid molecule (II) comprising a polynucleotide sequence encoding (I);

(5) a vector comprising (II); and

(6) a host cell comprising (II).

ACTIVITY - Cytostatic; anorectic; immunosuppressive; antidiabetic; antirheumatic; antiarthritic; psoriatic. No supporting data is given.

MECHANISM OF ACTION - None given.

USE - **Albumin** fusion proteins are stabilized therapeutic proteins e.g. antibodies to C5, C242 and CD80 useful for treating various diseases and disorders such as non-Hodgkin's lymphoma, cancer, obesity, transplant rejection, type I diabetes mellitus, rheumatoid arthritis and psoriasis.

ADVANTAGE - Fusing **albumin** to therapeutic proteins stabilizes the therapeutic protein, extends the shelf life and retains the in vitro or in vivo biological activity. It also reduces the need to formulate protein solutions with large excesses of carrier proteins to prevent loss of therapeutic proteins due to factors such as binding to the container. The fusion proteins are easily dispensed with a simple formulation requiring minimal post storage manipulation.

The fusion of therapeutic proteins to **albumin** confers stability in aqueous or other solution. A solution of 200 microgram/ml of human **albumin** (HA)-human growth hormone (hGH) was prepared in tissue culture media containing 5% horse serum and the solution incubated at 37 degrees C starting at time zero. A sample was removed and tested for its biological activity in the Nb2 cell assay at 2 ng/ml final concentration. The biological activity of HA-gHG remained essentially intact after 5 weeks of incubation at 37 degrees C. The recombinant hGH used as control lost its biological activity in the first week of the experiment.

Dwg.0/20

FS CPI

FA AB; DCN

MC CPI: B04-B04D4; B04-E02F; B04-E03A; B04-E08; B04-F0100E; B04-G01; **B04-N02B0E**; B04-P0100E; B11-C07A; B12-K04A; B14-C09B; B14-E12; B14-G02C; B14-H01; B14-N17C; B14-S04; D05-H11; D05-H12A; D05-H12C; D05-H12E; D05-H14; D05-H16; D05-H17C; D05-H17C1

TECH UPTX: 20011129

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Protein: The **albumin** activity is the ability to prolong the shelf life of the therapeutic protein: X compared to the shelf life of therapeutic protein: X in the unfused state. (I) has a greater shelf life than the therapeutic protein: X in the unfused state. The in vitro or in vivo biological activity of (I) is greater than the in vitro or in vivo activity of therapeutic protein: X or its fragment or variant in an unfused state. (I) comprises 2 therapeutic protein: X or their fragments or variants, which are different from each other. Therapeutic protein: X or its fragment or variant is separated from the **albumin** or its fragment or variant by a linker. (I) comprises a therapeutic protein: X or its fragment or variant I-inserted into an **albumin** comprising amino acids 54-61, 76-89, 92-100, 170-176, 247-252, 266-277, 280-288, 362-368, 439-447, 462-475, 478-486 or 560-566 of S18. (I) further comprises a secretion leader sequence. (I) has the formula: R1-L-R2; R2-L-R1; or R1-L-R2-L-R1, where:

R1 = therapeutic protein: X or its fragment or variant;
L = peptide linker; and
R2 = **albumin** comprising S18.
(I) is non-glycosylated and expressed in a glycosylation and protease deficient yeast cell. Alternatively (I) is expressed in a mammalian cell in culture.
Preferred Method: The disease or disorder comprises indication: Y.
Preparation: (I) are prepared by standard recombinant techniques.
ABEX UPTX: 20011129
WIDER DISCLOSURE - Also disclosed as new are:
(1) transgenic organisms modified to contain (II) to express (I);
(2) antibodies that bind to a therapeutic protein;
(3) generating antibodies that bind to a therapeutic protein;
(4) polynucleotides encoding the antibody;
(5) diagnosing a disorder comprising assaying the expression of the therapeutic protein in cells or body fluid of an individual using antibodies specific to the therapeutic protein and comparing the level of gene expression with a standard gene expression level, where an increase or decrease in the assayed gene expression level is indicative of a particular disorder; and
(6) a diagnostic kit for use in screening serum containing antigens of a therapeutic protein comprising an antibody immunoreactive with the antigen.

ADMINISTRATION - 0.1-100 mg/kg of body weight, preferably 1-10 mg/kg of body weight of antibodies are administered by standard routes.

EXAMPLE - Preparation of human **albumin** fusion proteins was as follows. The cDNA for interferon (IFN) alpha was isolated from cDNA libraries by reverse transcription-polymerase chain reaction (PCR) and by PCR using a series of overlapping synthetic oligonucleotides primers using standard methods. The cDNA was tailored at the 5' and 3' ends to generate restriction sites so that oligonucleotide linkers could be used to clone the cDNA into a vector containing the cDNA for human **albumin** (HA). This could be at the N or C terminus of the HA sequence with(out) use of a spacer sequence. The IFN alpha cDNA was cloned into a vector such as pPPC0005 from which the complete expression cassette was excised and inserted into the plasmid pSAC35 to allow the expression of the **albumin** fusion protein in yeast. The **albumin** fusion protein was collected and purified from the media and tested for its biological activity.

L88 ANSWER 5 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN **2001-602931** [68] WPIX
CR 2001-611723 [70]; 2001-616754 [71]; 2001-616755 [71]; 2001-616756 [71]; 2002-010886 [01]; 2002-179329 [23]; 2003-810996 [76]; 2004-033644 [03]
DNC **C2001-178694**
TI **Albumin** fusion proteins comprising a therapeutic protein and **albumin**, useful in the treating metastatic renal cell carcinoma, metastatic melanoma, malignant melanoma, renal cell carcinoma, HIV (human immunodeficiency virus) or infection.
DC B04 D16
IN PRIOR, C P; **ROSEN, C A**; SADEGHI, H; TURNER, A J
PA (HUMA-N) HUMAN GENOME SCI INC; (PRIN-N) PRINCIPIA PHARM CORP; (PRIO-I) PRIOR C P; (ROSE-I) ROSEN C A; (SADE-I) SADEGHI H; (TURN-I) TURNER A J
CYC 96
PI WO 2001079258 A1 20011025 (200168)* EN 325p C07K001-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001059066 A 20011030 (200219) C07K001-00
EP 1274720 A1 20030115 (200313) EN C07K001-00
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
US 2003171267 A1 20030911 (200367) A61K038-38 <--
JP 2003530838 W 20031021 (200373) 430p C12N015-09

ADT WO 2001079258 A1 WO 2001-US12008 20010412; AU 2001059066 A AU 2001-59066 20010412; EP 1274720 A1 EP 2001-932549 20010412, WO 2001-US12008 20010412; US 2003171267 A1 Provisional US 2000-229358P 20000412, Provisional US 2000-199384P 20000425, Provisional US 2000-256931P 20001221, US 2001-833117 20010412; JP 2003530838 W JP 2001-576855 20010412, WO 2001-US12008 20010412

FDT AU 2001059066 A Based on WO 2001079258; EP 1274720 A1 Based on WO 2001079258; JP 2003530838 W Based on WO 2001079258

PRAI US 2000-256931P 20001221; US 2000-229358P 20000412; US 2000-199384P 20000425; US 2001-833117 20010412

IC ICM **A61K038-38**; C07K001-00; C12N015-09
ICS A01N037-18; A61K035-12; A61K035-76; A61K038-00; **A61K038-21**; A61K038-22; A61K038-23; A61K038-27; A61K047-48; A61K048-00; A61P001-04; A61P003-10; A61P003-14; A61P005-10; A61P009-10; A61P015-08; A61P017-00; A61P017-02; A61P017-06; A61P017-14; A61P019-00; A61P019-02; A61P019-08; A61P019-10; A61P021-00; A61P025-00; A61P025-02; A61P025-28; A61P029-00; A61P031-14; **A61P031-18**; A61P031-20; A61P035-00; A61P035-02; A61P035-04; A61P037-00; A61P037-06; C07K014-55; C07K014-565; C07K014-585; C07K014-60; C07K014-62; C07K014-635; C07K014-76; C07K014-765; C07K019-00; C12N001-19; C12N005-10

AB WO 200179258 A UPAB: 20040112
NOVELTY - **Albumin** fusion proteins (P1) comprising a therapeutic protein (T1) (or its fragment or variant having the activity of T1) and **albumin** comprising the 585 amino acid sequence (I) defined in the specification (or its fragment or variant having **albumin** activity), are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a kit comprising a composition containing P1;

(2) a method of treating a disease or disorder, preferably modulated by T1, in a patient, comprising administering P1;

(3) a method of extending the shelf-life of T1, comprising fusing T1 or its fragment or variant, to **albumin** or its fragment or variant, where the shelf-life of T1 or its fragment or variant as part of a fused protein is extended when compared to T1 or its fragment or variant in an unfused state;

(4) a nucleic acid (N1) comprising a nucleotide sequence encoding P1;

(5) a vector comprising N1; and

(6) a host cell comprising N1.

ACTIVITY - Cytostatic; antiviral; antiinflammatory; antileukemic; antiarthritic; antirheumatic; immunosuppressive; antidiabetic; cardiant; nootropic; neuroprotective; antimicrobial; vulnerary.

To test whether sympathetic neuronal cell viability is supported by an **albumin** fusion protein, the chicken embryo neuronal survival assay (Senaldi, et al., Proc. Natl. Acad., Sci., U.S.A, 96:11458-63 (1998)). Briefly, motor and sympathetic neurons were isolated from chicken embryos, resuspended in L15 medium (with 10% fetal calf serum (FCS), glucose, sodium selenite, progesterone, **conalbumin**, putrescine and insulin) and Dulbecco's modified Eagles medium (with 10% FCS, glutamine, penicillin, and 25 mM Hepes buffer (pH 7.2)), respectively and incubated at 37 degrees Centigrade in 5% carbon-dioxide in the presence of different concentrations of the purified fusion protein, as well as negative control lacking any cytokine, After 3 days, neuronal survival was determined by evaluation of cellular morphology, and through the use of the colorimetric assay of Mosmann (Mosmann, T., J. Immunol., Methods, 65:55-63 (1983)). Enhanced neuronal cell viability as compared to the

controls lacking cytokine is indicative of the ability of the **albumin** fusion protein to enhance the survival of neuronal cells.

MECHANISM OF ACTION - Gene therapy.

USE - When the therapeutic protein, or its fragment or variant is IL-2, P1 is used to treat metastatic renal cell carcinoma, metastatic melanoma, malignant melanoma, renal cell carcinoma, HIV (human immunodeficiency virus) infection, inflammatory bowel disorder, Kaposi's sarcoma, leukemia, multiple sclerosis, rheumatoid arthritis, transplant rejection, type 1 diabetes mellitus, lung cancer, acute myeloid leukemia, hepatitis C, non-hodgkin's lymphoma or ovarian cancer (claimed).

The **albumin** fusion proteins are also useful in the treatment, prevention, diagnosis, and/or detection of diseases, disorders such as immune system disorders (e.g. transplant rejection), blood related disorders (e.g. myocardial infarction), hyperproliferative disorders (e.g. childhood acute myeloid leukemia), renal disorders (e.g. glomerulonephritis), cardiovascular disorders (e.g. arrhythmias), respiratory disorders (e.g. non-allergic rhinitis), neurological diseases (e.g. Alzheimer's disease), endocrine disorders (e.g. pheocytochroma), reproductive system disorders (e.g. syphilis), infectious diseases (e.g. measles), gastrointestinal disorders (e.g. irritable bowel syndrome) and wound healing.

Dwg.0/14

FS CPI

FA AB; DCN

MC CPI: **B04-C01**; B04-E02F; B04-E08; B04-F0100E; B04-F1100E; **B04-H05**; B04-H06; B04-J04; **B04-N0200E**; **B04-N02A0E**; B14-A02B1; B14-C09B; B14-D01; B14-E10C; B14-F01; B14-F02; B14-G02; B14-H01; B14-J01; B14-K01; B14-N10; B14-N12; B14-N14; B14-N17B; B14-S01; B14-S03; B14-S04; **D05-H12B2**; D05-H12E; D05-H14

TECH UPTX: 20011121

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Fusion Protein: The **albumin** activity is the ability to prolong the shelf-life of T1 compared to the shelf-life of T1 in an unfused state. The **albumin** fragment or variant comprises amino acids 1-387 of (I). T1 comprises interleukin 2 (IL-2). The T1 fragment or variant has T cell proliferative activity or T cell activation activity. T1 or its fragment or variant, comprises a protein selected from calcitonin, growth hormone releasing factor, IL-2 fusion protein, insulin-like growth factor-1, **interferon beta** or parathyroid hormone. T1 or its fragment or variant is fused to the C-terminal of the **albumin** or the C-terminus of the fragment or variant of **albumin**. Alternatively, T1 or its fragment or variant is fused to the N-terminal of the **albumin** or the N-terminus of the fragment or variant of **albumin**. Alternatively, T1 or its fragment or variant is fused to the N-terminus and C-terminus of the **albumin**, or the N-terminus and C-terminus of the fragment or variant of **albumin**.

P1 comprises a first T1 or its fragment or variant, and a second T1 or its fragment or variant, where the first T1 is different from the second T1. T1 or its fragment or variant is separated from the **albumin** or the fragment or variant of **albumin** by a linker. Preferably, P1 is of the formula (S1), (S2) or (S3).

R1-L-R2 (S1);

R2-L-R1 (S2); or

R1-L-R2-L-R1 (S3).

where

R1 = is T1 or its fragment or variant;

L = is a peptide linker; and

R2 = is **albumin** comprising the sequence of (I), or its fragment or variant.

The shelf-life of the **albumin** fusion protein is greater than the shelf-life of T1 or its fragment or variant in an unfused state. The in vitro or in vivo biological activity of T1 or its fragment or

variant, fused to **albumin** or its fragment or variant, is greater than the in vitro or in vivo, respectively, biological activity of T1 or its fragment or variant, in an unfused state.
Alternatively, P1 comprises T1 or its fragment or variant, inserted into an **albumin** comprising the sequence of (I) or its fragment or variant. Preferably, the **albumin** comprises residues 54-61, 76-89, 92-100, 170-176, 247-252, 266-277, 280-288, 362-368, 439-447, 462-475, 478-486, or 560-566 of (I). The portion of **albumin** is sufficient to prolong the shelf-life and in vitro and in vivo biological activity of T1 or its fragment or variant, as compared to the shelf-life and in vitro and in vivo biological activity of T1 or its fragment or variant, in an unfused state.
P1 is non-glycosylated and expressed in yeast which is glycosylation deficient. The yeast may also be protease deficient. Alternatively, P1 is expressed by a mammalian cell in culture. P1 further comprises a secretion leader sequence.

ABEX UPTX: 20011121

ADMINISTRATION - The **albumin** fusion proteins can be administered orally, rectally, parenterally, intracisternally, intravaginally, intraperitoneally, topically, bucally, or as an oral or nasal spray. The dosage is 1 microgram/kg/day to 10 mg/kg/day, preferably 0.01 to 1, mg/kd/day. If given continuously, the **albumin** fusion protein is typically administered at a dose rate of 1-50 micrograms/kg/hour, either by 1-4 injections per day or by continuous subcutaneous infusions.

EXAMPLE - The cDNA for the growth factor of interest such as interferon growth factor 1 (IGF-1) can be isolated using a variety of means including but not exclusively, from cDNA libraries, by reverse transcriptase-polymerase chain reaction (PCR) and by PCR using a series of overlapping synthetic oligonucleotide primers, all using standard methods (see GenBank Acc. Number NP-000609). The cDNA can be tailored at the 5' and 3' ends to generate restriction sites, such that the oligonucleotide linkers can be used, for cloning of the cDNA into a vector containing the cDNA for human serum **albumin** (HA). This can be a the N or C-terminus with or without the use of a spacer sequence. The growth factor cDNA was cloned into a vector such as pPPC0005, pScCHSA, pScNHSA or pC4:HSA from which the complete expression cassette is then excised and inserted into the plasmid pSAC35 to allow the expression of the **albumin** fusion protein in yeast. The **albumin** fusion protein secreted from the yeast can then be collected and purified from the media and tested for its biological activity. For expression in mammalian cell lines a similar procedure is adopted except that the expression cassette used employs a mammalian promoter, leader sequence and terminator. This expression cassette is then excised and inserted into a plasmid suitable for the transfection of mammalian cell lines.

L88 ANSWER 6 OF 6 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN **1996-300388** [30] WPIX
DNC **C1996-095415**
TI New chimeric proteins for treatment of septic shock, psoriasis, cancers etc. - comprise cytokine bonded to polypeptide which is enzymatically inactive in humans, increases half-life and prevents cytokine(s) from crossing blood brain barrier.
DC B04
IN STEELE, A; STROM, T B; ZHENG, X; ZHENG, X X
PA (BETH-N) BETH ISRAEL HOSPITAL ASSOC
CYC 20
PI WO 9618412 A1 19960620 (199630)* EN 58p A61K038-19
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: CA JP
EP 793504 A1 19970910 (199741) EN A61K038-19
R: CH DE FR GB IT LI SE
JP 11501506 W 19990209 (199916) 49p C12N015-09

US 6403077 B1 20020611 (200244) A61K038-20
US 6410008 B1 20020625 (200246) C07K014-54
US 2002173628 A1 20021121 (200279) A61K038-52
US 2003026778 A1 20030206 (200318) A61K038-20

ADT WO 9618412 A1 WO 1995-US16046 19951212; EP 793504 A1 EP 1995-943058 19951212, WO 1995-US16046 19951212; JP 11501506 W WO 1995-US16046 19951212, JP 1996-519191 19951212; US 6403077 B1 CIP of US 1994-355502 19941212, Cont of US 1995-431535 19950428, US 1997-968905 19971106; US 6410008 B1 US 1994-355502 19941212; US 2002173628 A1 Cont of US 1994-355502 19941212, US 2002-145481 20020514; US 2003026778 A1 CIP of US 1994-355502 19941212, Cont of US 1997-968905 19971106, US 2002-145517 20020514

FDT EP 793504 A1 Based on WO 9618412; JP 11501506 W Based on WO 9618412; US 2002173628 A1 Cont of US 6410008; US 2003026778 A1 Cont of US 6403077, CIP of US 6410008

PRAI US 1995-431535 19950428; US 1994-355502 19941212; US 1997-968905 19971106; US 2002-145481 20020514; US 2002-145517 20020514

REP 2.Jnl.Ref; US 5231012

IC ICM A61K038-19; A61K038-20; A61K038-52; C07K014-54; C12N015-09
ICS A61K038-00; **A61K038-21**; **A61K038-38**; A61K039-395; **C07K014-52**; C07K014-525; C07K014-53; C07K014-535; C07K014-545; C07K014-55; **C07K014-555**; **C07K014-76**; **C07K014-765**; C07K016-18; C07K016-46; **C07K019-00**; C12N009-10; C12N015-02; C12N015-24; C12P021-02

AB WO 9618412 A UPAB: 19960731
Chimeric protein comprises a cytokine bonded to a polypeptide which is enzymatically inactive in humans and which increases the circulating half-life of the cytokine in vivo by a factor of 1.

Also claimed is the use of interleukin-10 (IL-10)/Fc in the preparation of a medicament for inhibiting granuloma formation in a patient.

USE - The chimeric proteins can be used to treat conditions for which the corresp. cytokines are used, e.g. septic shock, granulomatous disorders (e.g. schistosomiasis), multiple sclerosis, psoriasis, rheumatoid arthritis, cancers and virus infections. Chimeric proteins including a lytic Fc region can also be used to deplete patients of suppressor lymphocytes and to treat chronic infections such as those associated with suppression of the immune system.

ADVANTAGE - The enzymatically inactive polypeptides extend the circulating half-life of the cytokines in vivo by a factor of 10 (claimed). In addition, they can prevent the cytokines from crossing the blood brain barrier and causing adverse side effects.

Dwg.0/15

FS CPI
FA AB
MC CPI: B04-B04; B04-G01; B04-H02; B04-H04A; B04-H04C; B04-H08; **B04-N02**; B14-A01; B14-C09B; B14-N17C; B14-S01; B14-S06

=> => d his

(FILE 'HOME' ENTERED AT 15:22:31 ON 02 FEB 2004)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 15:22:50 ON 02 FEB 2004
E ALBUMIN/CT
L1 753 S E3
L2 132 S E11
E E47+ALL
L3 80101 S E2+NT
E E33+ALL
L4 566 S E3,E2
L5 25218 S E2+NT
L6 157881 S ?ALBUMIN?

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L7       181833 S L1-L6
L8         2969 S BDNF OR BD NF
L9         2881 S BRAIN DERIVED NEUROTROPHIC FACTOR
L10        2883 S (BD OR BRAIN DERIVED)()(NF OR NEUROTROPHIC FACTOR)
                E NEUROTROPHIC FACTOR/CT
L11         141 S E10
L12        2554 S E26
                E E25+ALL
L13         789 S E3-E5 AND BRAIN DERIVED
L14         679 S E12,E13
L15        3242 S E2+NT (L) BRAIN DERIVED
L16          64 S L7 AND L8-L15
L17       19234 S INTERFERONALPHA OR ALPHAINTERFERON OR INTERFERONBETA OR BETAI
                E INTERFERON/CT
L18         302 S E3-E19
L19       18390 S E85-E101
                E INTERFERONS/CT
                E E3+ALL
L20       18391 S E7,E6 (L) (ALPHA OR BETA)
L21         546 S L7 AND L17-L20
L22        2340 S TIMP()(I OR 1)

     FILE 'REGISTRY' ENTERED AT 15:29:36 ON 02 FEB 2004
L23            1 S 140208-24-8

     FILE 'HCAPLUS' ENTERED AT 15:30:37 ON 02 FEB 2004
L24         2026 S L23
L25          859 S TISSUE INHIBITOR(1W)METALLOPROTEINASE 1
L26           27 S METALLOPROTEINASE INHIBITOR 1
L27          651 S TIMP1
L28           12 S FIBROBLAST COLLAGENASE INHIBITOR
L29           91 S L7 AND L22,L24-L28
L30          678 S L16,L21,L29
L31         9815 S IFNALPHA OR IFNBETA OR ALPHAIFN OR BETAIFN OR IFN(A)(ALPHA OR
L32          119 S L7 AND L31
L33          700 S L30,L32
L34           62 S L33 AND (FUSION OR FUSE OR FUSED OR FUSES OR FUSING)
L35          167 S L33 AND RECOMBIN?
L36           44 S L33 AND CHIMER?
L37          202 S L34-L36
                E ROSEN C/AU
L38           27 S E3,E4
                E ROSEN CRAIG/AU
L39          625 S E3-E5
                E HASELTINE W/AU
L40          302 S E3,E4,E7-E10
L41           10 S L33 AND L38-L40
                E HUMAN GENOME SCI/PA,CS
L42          975 S E5-E37
L43           13 S L33 AND L42
L44           13 S L41,L43
L45           13 S L44 AND L37
L46            9 S L45 AND (SHELFLIFE OR SHELF LIFE)
L47            4 S L45 NOT L46
                SEL DN AN 1 4
L48            2 S L47 NOT E1-E6
L49           11 S L46,L48
                SEL RN
                DEL SEL
                E FUSION PROTEIN/CT
L50       11933 S E9
                E E9+ALL
L51        3795 S E3,E4
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L52           5 S L51 AND L33
L53          29 S L50 AND L33
L54          34 S L49,L52,L53
L55          27 S L54 AND ALBUMIN
L56           7 S L54 NOT L55
L57         159 S L37 AND ALBUMIN
L58         132 S L57 NOT L43-L49,L52-L56
L59           6 S L58 AND L16
L60           7 S L58 AND L29
L61         121 S L58 NOT L59,L60
L62          96 S L61 AND (PD<=20000412 OR PRD<=20000412 OR AD<=20000412)
                SEL DN AN 9 12 13 24 29 31 35 39 44 47 55 58 72 74 83 85 92 93
L63          18 S L62 AND E1-E54
L64          29 S L49,L63 AND L1-L22,L24-L63
L65          29 S L64 AND ?ALBUMIN?
L66          29 S L64 AND (INF? OR INTERFERON OR TIMP? OR NEUROTROPHIC?)

     FILE 'HCAPLUS' ENTERED AT 16:00:16 ON 02 FEB 2004

     FILE 'WPIX' ENTERED AT 16:01:33 ON 02 FEB 2004
L67        9861 S L6/BIX
L68         318 S L8/BIX OR L9/BIX OR L10/BIX
L69        1564 S L17/BIX OR LL31/BIX
L70          80 S L22/BIX OR L25/BIX OR L26/BIX OR L27/BIX OR L28/BIX
L71         124 S L67 AND L68-L70
L72       11209 S ?ALBUMEN?/BIX OR L67
L73         513 S (A61K038-38 OR C07K014-76 OR C07K014-765 OR C12N015-14)/IC,IC
L74       11377 S L72,L73
L75        2983 S V275/M0,M1,M2,M3,M4,M5,M6 OR (B02-V03 OR C02-V03 OR B04-H05A
L76        2604 S (A61K038-21 OR C07K014-52 OR C07K014-555 OR C07K014-56 OR C07
L77         216 S L74 AND L75
L78         111 S L74 AND L76
L79         129 S L74 AND L68,L69,L70
L80         311 S L77-L79
L81           3 S L80 AND (ROSEN C? OR HASELTINE W?)/AU
L82        7242 S (D05-H12B OR D05-H12B2)/MC
L83       58614 S (B04-C01? OR C04-C01? OR B04-N02? OR C04-N02?)/MC
L84         144 S L80 AND L82,L83
L85          15 S C07K019/IC,ICM,ICS AND L84
                SEL DN AN 1 4 5 6 7 12
L86           6 S E55-E66 AND L85
L87           6 S L81,L86
L88           6 S L87 AND L67-L87

     FILE 'WPIX' ENTERED AT 16:25:05 ON 02 FEB 2004

     FILE 'HCAPLUS' ENTERED AT 16:25:16 ON 02 FEB 2004

     FILE 'REGISTRY' ENTERED AT 16:26:59 ON 02 FEB 2004
L89           1 S 507485-69-0
L90           1 S 472960-22-8

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